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THE NERVOUS AND CHEMICAL CONTROL OF SWEATING.*

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THE work of Kuno (1934) has shown that there are two fundamentally different types of stimuli which evoke two quite different types of sweat response. *Heating* the body leads to profuse sweating, which is most marked on the forehead, dorsum of the hand, and chest and neck, and is least in the palm of the hand and the sole of the foot. On the other hand a *mental, emotional* or *sensory* stimulus produces sweating which is largely confined to the palms and soles, though it may also occur in the axillae. Both types of sweating are entirely under the control of the central nervous system, thermal sweating by the temperature-regulating centre in the anterior portion of the hypothalamus and mental sweating by centres not yet accurately localized, but possibly situated in the cerebral cortex (Fig. 1). These centres act *via* descending pathways within the central nervous system which finally relay around connector cells belonging anatomically to the sympathetic system, and therefore situated in the lateral horn of grey matter between the 1st thoracic and 2nd lumbar segments respectively of the spinal cord. After transection of the spinal cord these cells may function independently to produce the profuse sweating characteristic of the " mass reflex " response.

The connector cells give rise to preganglionic nerve fibres which leave the spinal cord, in company with other sympathetic fibres, *via* the anterior roots, and run thence to the sympathetic chain. Eventually these preganglionic

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fibres relay in a sympathetic ganglion whose nerve cells connect with the sweat glands by means of postganglionic fibres which pass to their destination along mixed or sensory nerves.

From the anatomical viewpoint the innervation of the sweat glands thus forms part of the sympathetic nervous system, but it has long been known that the responses of these glands to drugs closely resemble those of glands

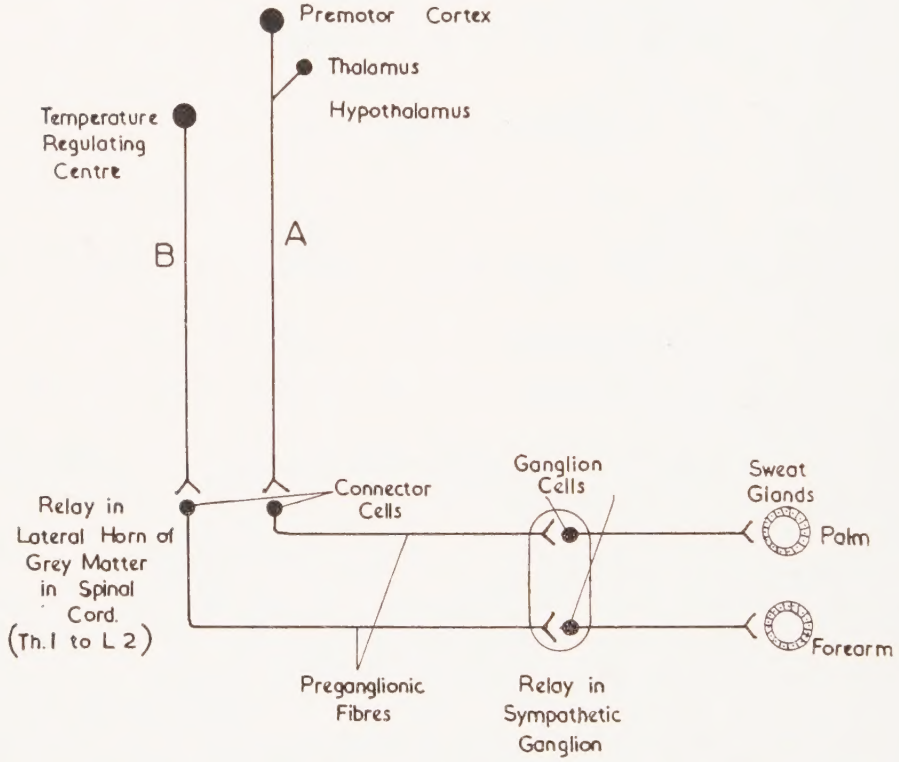

FIG. 1.—A: Pathway from cerebral cortex to sweat glands of palm. These are representative of the glands which take part in "emotional" sweating. B: Pathway from temperature regulating centre in hypothalamus to forearm.

under the control of the parasympathetic nervous system. Like the salivary and mucous glands, which are innervated by the latter system, sweat glands are excited by acetylcholine and pilocarpine, and are inhibited by atropine. This resemblance was explained when Dale and Feldberg (1934) showed that acetylcholine was (as is also the case at all postganglionic parasympathetic nerve terminals) the chemical transmitter between the endings of the sweat nerve fibres and the sweat glands. Nearly all the other sympathetic postganglionic fibres liberate adrenaline or *nor*adrenaline (or both) as chemical transmitter. Dale has clarified the situation by calling nerve fibres which

liberate acetylcholine at their terminals "cholinergic" and those which liberate adrenaline "adrenergic." Thus all postganglionic parasympathetic fibres are cholinergic and the great majority of postganglionic sympathetic fibres adrenergic, but those which control the sweat glands are cholinergic.

The liberation of acetylcholine at the cholinergic nerve endings only occurs in response to the arrival of a nerve impulse. An increase in the number of nerve impulses sent out from the centres leads to an increase in the quantity of acetylcholine released at the nerve endings and so to increased secretion of sweat. The intensity, and even more the duration, of response to acetylcholine is determined also by the rate of removal of the substance from its site of action. This removal is effected partly by simple diffusion, but chiefly by means of the destruction of acetylcholine by the enzyme *cholinesterase*, which is found in all regions supplied by cholinergic nerves. Drugs which inhibit cholinesterase, e.g., eserine and neostigmine (prostigmine), allow acetylcholine to build up to higher concentrations around cholinergic nerve endings and thus enhance the responses of organs controlled by such nerves. On the other hand atropine, which inhibits the response of many organs to cholinergic nerve stimulation, in some way prevents acetylcholine from making contact with the receptors at the surface of the responding tissue, such contact being a necessary preliminary to physiological action.

Abnormal increases in activity of autonomically innervated organs might arise in two main ways. On the one hand there might be excessive activity on the part of the controlling centres in the nervous system, and on the other there might be an excessive response by the innervated organ to normal amounts of chemical transmitter. In other words the abnormality might reside either in the central controlling mechanism or in the peripheral responding organ.

This type of problem was clearly discussed by Lewis (1936) in his work on Raynaud's syndrome, where the question arose as to whether the abnormal vasoconstriction elicited by exposure to cold was due to excessive vasomotor nerve activity, or to a direct enhanced sensitivity of the smooth muscle of the affected vessels to temperatures not low enough to cause vasoconstriction in normal people. Lewis was able to show that in Raynaud's syndrome there was generally a direct increased sensitivity to cold on the part of the arteries of the palmar arch and digital arteries. Thus in this instance the abnormality in response seems to be a property of the peripheral structure and not of the nervous control.

This work of Lewis's led us to consider the possibility that essential hyperidrosis might be due to an increased sensitivity of the hyperactive sweat glands to the chemical transmitter acetylcholine, and this in turn raised the question as to how we could best assess the relative contribution of central control and peripheral sensitivity to abnormalities of function.

We first tried to study the responses of sweat glands in normal persons to intravenous infusions of either acetylcholine (up to 75 mg. per minute) or methacholine (acetyl-β-methylcholine, Mecholyl, given at rates up to 0·30 mg. per minute), but we were unable to produce sweating in the forearms and hands, in which we were primarily interested, even when marked flushing of the skin, salivation and tightness in the chest developed.

We therefore began to study the responses of the sweat glands in the forearm and palm to local injections of acetylcholine, which we considered preferable to other sudorific substances such as pilocarpine, since it is the natural chemical transmitter. The acetylcholine solution was given by deep intradermal injection, so as to get as near to the sweat glands as possible and, before giving the injection, the needle was pushed along in the skin for about 1 cm. so that the sweat-gland activity could be measured in unpunctured skin. The volume of injected solution (usually 0·01 ml.) was accurately measured by means of an " Agla " micrometer syringe.

The tests were carried out with the subject resting on a couch. The room temperature was usually between 18° and 20° C. We recorded sweat gland activity in two ways :

(i) By measuring the electrical resistance of the skin, as suggested by Richter and Levine (1937).

(ii) By counting the number of active sweat glands using Randall's (1946) iodine-starch paper method.

For the measurement of electrical resistance a saline pad incorporating a chlorided silver wire was strapped to the upper arm, and a silvered brass disc 15 mm. in diameter, with a non-conducting handle, was applied lightly to the skin. A 9-volt battery and a sensitive galvanometer (0–24 μA) completed the circuit. The presence of sweat on the skin surface greatly reduces the electrical resistance. The measure of this reduction is the current flow through the galvanometer.

Randall's method for recording sweating is briefly as follows : the skin is painted with 3% iodine in 95% alcohol and a piece of starch paper is applied to the test area. Each active sweat gland shows as a tiny dark blue point on the paper. The number of dots can be counted with a lens, and the size of the dots gives some measure of the rate of secretion of individual glands.

Responses to Intradermal Acetylcholine.

Coon and Rothman (1941) have stated that locally injected acetylcholine may stimulate the sweat glands by two mechanisms : (*a*) a direct muscarine-like action on the gland cells, (*b*) a nicotine-like action on nerve endings causing sweating by means of an axon reflex. We have never been convinced that the sweating which we observed (with acetylcholine concentrations of 10^{-7}

to 10^{-2}) was due to any mechanism other than the muscarine-like action, since there was always a latent period before sweating occurred and the distribution of active glands was that to be expected from diffusion of intradermally injected acetylcholine. We have occasionally seen reflex pilomotor stimulation with 10^{-2} to 10^{-4} acetylcholine, and we have confirmed that nicotine can cause immediate, reflex sweating. The absence of nicotine-like stimulation of sweating with acetylcholine may have been due to the small volume of injected solution which we used in our experiments.

Typical responses to the injection of acetylcholine into the forearm are shown in Table I, in which it can be seen that the measurements of sweat

Sweat response to intradermal injection of acetylcholine in the forearm.

Injection.	Starch paper (No. of dots).	Electrical reading (Microamps).
Ach 10^{-6}	0	0
10^{-5}	3	0·2
10^{-4}	11	1·0

TABLE I.—*The Acetylcholine Concentration is Expressed in Grammes per Millilitre, e.g., Ach* 10^{-6} *means Ach* $1/10^6 = 1$ *μg./ml. The number of dots recorded on the starch paper indicates the number of active sweat glands.*

gland activity by the starch paper and electrical resistance methods agree very closely. The data in this table also show how the *threshold* sensitivity to acetylcholine can be measured. It will be seen that there is no response to 10^{-6} of the drug, and a small but definite response to 10^{-5} acetylcholine, which in this case would be called the *threshold* value. The threshold concentration in the skin of the forearm very rarely shows more than a tenfold variation (e.g., from 10^{-5} to 10^{-4}) in any one subject when tested on different occasions, except that there is a tendency for an increase in sensitivity of sweat glands to acetylcholine during hot weather.

There are, however, wide variations in the sensitivity to acetylcholine of sweat glands in different subjects. Threshold values were determined in 50 normal young adults (25 of each sex). In 47 of these subjects the threshold lay in the range 10^{-3} to 10^{-6}, one subject responded to 10^{-7}, one required 10^{-2} and one failed to respond to 10^{-2} acetylcholine. In contrast to the findings of Gibson and Shelley (1948) and Kahn and Rothman (1942) there was no significant difference between the responses of the two sexes.

The explanation of these variations in responses to acetylcholine is not clear, but changes in threshold can be induced by certain drugs. Inhibitors of cholinesterase, such as eserine, neostigmine and tetraethylpyrophosphate (TEPP), reduce the rate of destruction of acetylcholine, and would therefore be expected to lower the threshold concentration of acetylcholine required to produce sweating. Table II shows how such a change in the threshold was

TABLE II.—*Effect on Acetylcholine Threshold of Inhibition of Cholinesterase by Prior Intradermal Injection of Tetraethylpyrophosphate (TEPP).*

0·1 ml. TEPP was injected 5 minutes before the injection of acetylcholine.

Injection.	With TEPP.		Without TEPP.	
	Starch paper.	Micro-amps.	Starch paper.	Micro-amps.
Ach 10^{-7}	4	0·5	..	..
10^{-6}	13	1·2	0	0
10^{-5}	..	..	3	0·2
10^{-4}	..	..	11	1·0

produced by a local injection of TEPP, the smallest effective concentration of acetylcholine falling from 10^{-5} to 10^{-7}. A reduction in threshold of this order is commonly produced by inhibition of cholinesterase, but even after such inhibition there are still wide variations in sensitivity, which shows that differences in cholinesterase activity do not account for the normally observed differences in acetylcholine threshold.

Atropine has the opposite effect on the acetylcholine threshold, and local or intravenous administration of this drug can raise the threshold considerably (Fig. 2). The fact that the threshold can be altered in the expected ways by these drugs shows that the technique of measuring threshold responses of sweat glands is a sound one, and that individual differences in sensitivity are genuine. We also thought that differences in the extent of spreading of the injected acetylcholine might influence the threshold, but prior injection of hyaluronidase (" spreading factor ") had no effect upon the threshold, though it did increase the number of glands which responded to the threshold dose of acetylcholine.

Acetylcholine Threshold in Essential Hyperidrosis.

We have studied the responses to acetylcholine of the sweat glands of the palm of the hand in six patients with essential hyperidrosis involving this region. Our purpose was to see whether there was an increased sensitivity to the chemical transmitter, acetylcholine, so it was necessary also to measure the acetylcholine threshold in the palms of normal subjects. Now there are two difficulties which arise in the study of palmar sweat gland responses to intradermal acetylcholine. First, there is continuous secretion from these glands which gives a variable background against which to measure the effect of injected acetylcholine. Second, the injection is more painful in the palm than in the forearm, and pain reflexly causes sweating in this very region (psychogalvanic reflex). To overcome these two obstacles the median nerve was blocked by injection of procaine just above the wrist, and the acetylcholine threshold was then determined in the usual way by injection of acetylcholine solution into the skin of the anaesthetic and anhydrotic area. We had

already ascertained that procaine block of a sensory nerve in the forearm had no effect on the acetylcholine threshold in this area, and we have assumed the same to hold also for the palm.

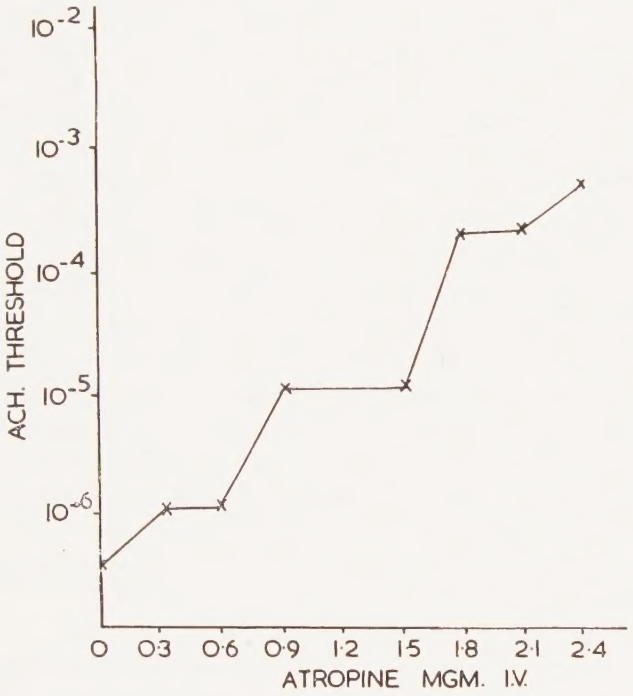

Fig. 2. Atropine was given by increments of 0·3 mgm. I.V. at 5 min. intervals There was a progressive rise in Ach threshold.

The results of this study are given in Table III. The range of the palmar acetylcholine threshold in 8 normal subjects was 10^{-3} to 10^{-8} and in 6 patients

TABLE III.—*Threshold Concentration of Acetylcholine for Stimulation of Palmar Sweat Glands in Normal and Hyperidrotic Subjects.*

Hyperidrotic subjects.		Normal subjects.	
B. F—	10^{-4}	I. G. H—	10^{-3}
Gr. S—	10^{-5}	A. C. P—	10^{-4}
S. C—	10^{-6}	A. A. G. L—	10^{-5}
I. S—	10^{-7}	G. du B.	10^{-5}
Gl. S—	10^{-7}	J. R—	10^{-7}
B. A. S—	10^{-8}	G. P. B—	10^{-7}
		J. A. F—	10^{-7}
		T. M. C—	10^{-8}

with hyperidrosis it was 10^{-4} to 10^{-8}. These findings have been published (Chalmers and Keele, 1949). It is clear that there is no difference between the two groups. If the hyperidrotic patients had all responded to acetylcholine in concentrations of 10^{-7} or 10^{-8} and the normal subjects only to concentrations of 10^{-3} to 10^{-4}, then one might have postulated that this greater sensitivity to the chemical transmitter might, at least in part, have contributed to the excessive secretion of sweat in the hyperidrotic patients. Since there was no such difference we must attribute the excessive activity of the sweat glands to excessive stimulation through the nervous pathway, but at present we do not know at what level in the central nervous system (or even perhaps in the sympathetic ganglia) such hyperactivity is located. It is interesting to note that in some patients with hyperidrosis there is an associated acrocyanosis, due probably to excessive vasomotor nerve activity to the arterioles of the affected skin. Since these latter nerves are adrenergic whereas those to sweat glands are cholinergic, it is certainly easier to accept the postulate of hyperactive centres than that of hypersensitive end organs to account for the excessive functional activity of structures which are both controlled by centres belonging to the sympathetic nervous system.

The Effects of Denervation on the Sensitivity of Sweat Glands to Acetylcholine.

We have already mentioned that procaine block of a sensory nerve does not alter the sensitivity to acetylcholine of the sweat glands in the anaesthetic area. We have also found that *preganglionic sympathectomy* in the upper limb does not significantly change the acetylcholine threshold in the sweat glands of the forearm. Table IV shows some results obtained in 5 patients

TABLE IV.—*Effect of Preganglionic Sympathectomy on Acetylcholine Threshold in Forearm.*

Subject.	Before operation.	5–14 days after operation.	14 days to 3 months after operation.	6–12 months after operation.
I. S—	10^{-6}	10^{-5}	..	10^{-6}
	..	10^{-5}	10^{-5}	10^{-6}
R. H—	10^{-5}	..	..	10^{-5}
	..	10^{-4}	..	10^{-4}
B. A. S—	10^{-4}	..	10^{-5}	10^{-5}
	..	..	10^{-6}	10^{-5}
H. M—	..	..	..	10^{-3}
J. Sch—	..	10^{-4}	..	..

(8 limbs in 5 subjects.)

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in whom all the acetylcholine threshold values lie in the normal range after section of the preganglionic sympathetic pathway. Moreover in 3 of these patients in whom pre-operative acetycholine thresholds were measured there were no significant changes in threshold after the operation.

After *ganglionectomy* with degeneration of the *postganglionic nerves* the situation appears to be different. Kahn and Rothman (1942) and Janowitz and Grossman (1950) have recorded diminished or absent sweat responses to intradermal acetylcholine after postganglionic sympathectomy, though there were no histological changes in the unresponsive glands. We have not been able to measure the acetylcholine threshold after postganglionic sympathectomy as this operation seems no longer to be performed. We have, however, had the opportunity of studying the responses in two patients with complete ulnar nerve section, in both of whom there was no response whatever when acetylcholine was injected into the anaesthetic area of palmar skin. In these patients the normal skin sweated profusely after injection of 10^{-4} acetylcholine, whereas the denervated skin was unresponsive to 10^{-2}.

The development of resistance to the action of the chemical transmitter after postganglionic denervation of the sweat glands is the converse of what happens in other autonomically innervated structures. The reason for this difference is not known.

Possible Adrenergic Innervation of Sweat Glands.

In some animals, e.g., the horse, the injection of adrenaline excites the sweat glands to secrete, whereas in other animals, e.g., the cat, secretion occurs only in response to acetylcholine. Recently Haimovici (1948) has made the suggestion that human sweat glands may have an adrenergic innervation, a view based on the finding that intravenous dibenamine (an adrenaline and sympathetic antagonist) reduced sweating in the palm. Sonnenschein *et al.* (1949) and Wada (1950) have further shown that intradermal injection of adrenaline in man can evoke local sweating even with concentrations down to 10^{-8}.

We have confirmed these findings concerning adrenaline, and Table V summarizes our results with adrenaline and dl-*nor*adrenaline compared with acetylcholine. It may be seen that the threshold sensitivity to adrenaline is similar to that of acetylcholine, though the response to the former was less marked, probably because of the accompanying vasoconstriction. *Nor*adrenaline appeared to behave like adrenaline.

Since human sweat glands respond to adrenaline, the possibility of their having an adrenergic innervation had to be considered. We studied this question in the following way : We first showed that this action of adrenaline is not due to release of acetylcholine, since atropine did not prevent it. Suitable concentrations of adrenaline antagonists were then shown to inhibit the

TABLE V.—*Threshold Concentration (to Produce Sweating) of l-Adrenaline, dl-Noradrenaline and Acetylcholine (Intradermal Injection in Forearm).*

Subject.	l-Adrenaline.	dl-*Nor*adrenaline.	Acetylcholine.
G. L. S. P—	10^{-7}	10^{-6}	5×10^{-6}
G. M—	10^{-4}	10^{-4}	10^{-4}
E. P. S—	10^{-6}	10^{-4}	10^{-5}
J. O—	10^{-3}	No response to 10^{-3}	10^{-3}
C. A. K—	10^{-3}	10^{-3}	10^{-4}
D. H. H—	No response to 10^{-3}	No response to 10^{-3}	No response to 10^{-2}
A. A. G. L—	10^{-5}	Not tested	10^{-5}
J. M—	10^{-6}	,,	10^{-5}
M. K. M—	10^{-4}	,,	10^{-4}
G. S—	10^{-5}	,,	10^{-4}
J. B. L. H—	No response to 10^{-3}	,,	10^{-3}
F. H—	10^{-5}	,,	10^{-6}

sweat-gland response to intradermal adrenaline. For example, when 0·2 ml. of a 10^{-2} solution of tolazoline (Priscol) was injected into an area of skin on the forearm, it completely prevented the response to 10^{-4} adrenaline injected 3 minutes later. The question then was whether tolazoline would inhibit thermal sweating in the same region of skin. To answer this an experiment was done as follows: Minor's method was used to demonstrate the sweat responses which were recorded by colour photography. In one arm atropine (10^{-4}) was injected locally, and in the other arm tolazoline (10^{-2}) was also injected locally, the volume of injected solution in both cases being 0·2 ml. Thermal sweating was then induced by immersing the legs in hot water. It was at once clear that whereas the area injected with atropine was entirely free of sweat, the area injected with tolazoline sweated as profusely as the uninjected areas on both arms. Thus a concentration of tolazoline which completely prevented the sweat response to local adrenaline had no influence on thermal sweating, which was, however, completely prevented by atropine. Therefore the nerve supply to the thermally active sweat glands of the forearm appears to be exclusively cholinergic.

We also studied the effects of such inhibitors on the emotional sweating of the palm. In this case secretion of sweat is continuous, and the inhibitors were administered by iontophoresis. The adrenaline inhibitor used was dihydroergocornine (DHO) in place of tolazoline. The effects were as clear-cut as on the forearm, atropine abolishing sweating and DHO having no

detectable action. These results have been published (Chalmers and Keele, 1951) and similar findings have been reported by Sonnenschein *et al.* (1951).

We may thus conclude that although the sweat glands which take part in both thermal and emotional sweating can be excited by adrenaline and *nor*adrenaline, there is no evidence whatever that adrenergic nerves play any part in the physiological control of sweating. Since the majority of post-ganglionic sympathetic nerves are adrenergic, and since their distribution to cutaneous blood vessels must place their endings very close to sweat glands there must be some barrier to the free diffusion of sympathetic transmitter. In conclusion we may say that in man the innervation of sweat glands appears to be entirely cholinergic.

Suppression of Sweating by Drugs.

The excessive palmar and plantar sweating in essential hyperidrosis can be controlled by *atropine*, but only in doses which also inhibit salivary secretion and may cause some disturbance of accommodation. Grimson *et al.* (1950) have reported favourably on another acetylcholine inhibitor, beta-diethyl-aminoethylxanthine-9-carboxylate methobromide (*banthine*), in the treatment of hyperidrosis. It is not yet clear, however, what advantages this substance has over atropine, since side effects such as dilatation of the pupil, dryness of the mouth and constipation have been noted.

We have recently treated six cases of hyperidrosis with *ganglionomic blocking agents* of the methonium group (Paton and Zaimis, 1948*a*, 1948*b*, 1951; Burt and Graham, 1950). In four of them preliminary intravenous injection of small doses (10–20 mg.) of pentamethonium or hexamethonium bromide produced partial suppression of sweating without side effects, such as postural hypotension. The average oral dose required was 250 mg. thrice daily. One subject did not respond to 500 mg. and it was decided not to exceed this dose; another discontinued treatment on account of headaches (which, however, were also produced by a control inert mixture). The other four patients were satisfied with the effect of the drug. After each dose the reduction of sweating appeared within 15 minutes and lasted 3 or 4 hours. Dummy tablets containing bromide only had no such effect. Three of these patients were young women who suffered from acrocyanosis as well as hyperidrosis: this symptom was also relieved by hexamethonium. The vasoconstriction had previously responded well to tolazoline (Priscol), which, however, had no effect on the sweating. The control of symptoms by hexamethonium was partial only, and in extremely cold or hot weather acrocyanosis or hyperidrosis was liable to return. No serious side effects were experienced. One patient had mild dragging headaches at first which passed off in 1–2 weeks with continued treatment, and another reported slight constipation. It is concluded that

small oral doses of hexamethonium are worth trying in cases of hyperidrosis before resorting to sympathectomy.

Much of the experimental work here described was included in a thesis presented by one of us (T.M.C.) for the degree of M.D.(Edin.).

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LIQUID NITROGEN IN THE TREATMENT OF WARTS.

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THE increasing incidence of warts in recent years is rendering their treatment a serious problem in busy clinics (Hellier, 1951). A report on the use of liquid nitrogen as a therapeutic agent of value in dealing with the condition is here presented.

Campbell White's report on the application of liquid air in medicine and surgery (1899) is the first record of the employment of a liquid gas as a freezing agent in treatment. In this and in a subsequent paper (1901) he gave accounts of its use in a diverse number of skin conditions. Whitehouse (1907) reported further on the subject, and stressed that with a good technique it was a very valuable agent. At that time liquid air was unobtainable commercially; with the introduction of carbon-dioxide snow by Pusey in 1907 a much more readily available freezing agent was provided, and the use of liquid air seems then to have lapsed. Nevertheless, Gold stated in 1910: ". . . as to the comparison of liquid air and carbon-dioxide snow, in every respect, where the opportunity of using both has been given, there is no hesitancy in saying that liquid air is far preferable."

However, by 1928 the practical difficulties of obtaining liquid gases no longer applied, and liquid oxygen was being produced in quantity commercially. In that year Irvine and Turnacliff reported on its use in 75 patients. They obtained good results in the treatment of warts and seborrhoeic keratoses, and emphasized that it provided a sure, quick and relatively painless method of removing warts; in addition, that it was equally efficient, more easily handled and less painful to apply than carbon-dioxide snow. They described a detailed technique for its use. Kile and Welsh (1948) reviewed the use of liquid oxygen in 1000 cases with substantially the same conclusions, and remarked that it gave a greater local reaction and was less time-consuming than the use of carbon-dioxide snow. Despite the Suttons' (1949) report of disappointing results, liquid oxygen seems to have been accepted as an effective freezing agent, but it does not appear to have been used extensively in this country. It was while liquid oxygen was being used in the treatment of warts, for which it proved most effective, that the manufacturers suggested to the author the substitution of pure liquid nitrogen. This gas is inert, and therefore does not carry with it the risk of fire, which is a major objection to oxygen. In 1950 Allington published a report on the use of liquid nitrogen in skin

diseases, and concluded that it was of sufficient value in the treatment of warts and keratoses to justify its adoption.

Liquid nitrogen is a by-product of the commercial preparation of oxygen for medical and industrial use, and is therefore readily available in urban areas. The industrial product is 99% pure, and is inexpensive, costing 5 shillings a quart. It is a colourless liquid boiling at — 195·8° C. at atmospheric pressure. As a freezing agent it therefore compares well with liquid oxygen, which boils at — 183° C., and with carbon-dioxide snow, which sublimates at — 78·5° C. (Hodgman, 1950). The liquid air used by earlier workers was a mixture of liquid oxygen and nitrogen, but the latter vaporized more rapidly, leaving nearly pure liquid oxygen. In the present work the liquid nitrogen has been obtained from the producers in an ordinary 2-pint vacuum flask which retains sufficient of its contents at room temperature to last about 72 hours. The flask must be left uncorked and loosely plugged with cotton wool, or the expansion of the vaporizing liquid will break it.* In this series the patients were all treated on a particular day each fortnight and the gas obtained on that morning, but by arranging a twice-weekly supply it should be possible to have liquid nitrogen available continuously if desired. Two pints will suffice to treat 50 or 60 patients.

Method.

The technique of its application does not differ from that described in detail for liquid oxygen. A cotton-wool swab or applicator is enclosed in a cardboard cylinder to obtain easy access into the flask.

The cotton wool should be saturated in the liquid ; freezing of the lesion then touched occurs almost instantaneously. Contact may need to be intermittent to avoid freezing a greater area than is desired. As the gas evaporates quickly, the applicator may need to be immersed in the liquid more than once, to obtain sufficient freezing. The required extent of freezing can be determined by the white appearance of the frozen area, and the rapidity with which it can be achieved varies with the thickness and extent of the lesion, ranging usually from 5 to 30 seconds. For small superficial warts and plane warts 5 seconds is usually enough, but on occasion deep-seated palmar and plantar warts may require as much as 60 seconds. The exact duration required for a given lesion is soon learnt by experience, the aim being to procuce a blister just sufficient to separate the wart from the surrounding tissues. With such a rapid effect large numbers of patients can be dealt with in a short time.

The application, although uncomfortable, is not sufficiently painful to upset children seriously, and less pain seems to be produced than with carbon-dioxide snow, probably because of the shorter duration of contact. Some pain is

* It has been found that glass flasks may fracture and disintegrate if allowed to become frozen around their mouths. To obviate this, care should be taken to avoid touching the rim with the applicator, or alternatively, a metal flask can be used.

felt for a time when the area thaws. Blistering occurs between 6 and 12 hours later. In this reported series the blisters have been opened and the warts removed after seven days. This operation is painless, but subsequent experience has shown that it is not necessary as the bullae dry up and exfoliate spontaneously, together with the warts, in about two weeks. The raw areas left from opening the blisters heal in a few days with dry dressings and in no case was sepsis observed. If the blisters are left unopened the epithelium heals under the scab before it comes away. Residual scarring is minimal and the final cosmetic result good.

Some warts, usually a small proportion of those in any particular patient, were not wholly removed with a single treatment, but became flatter and less horny; the majority of these responded to a second application. In only three cases was there any severe reaction in the nature of a single, unduly large, painful haemorrhagic blister, and these subsided uneventfully with simple dressings.

Results.

A total of 109 patients with 1059 warts were treated. Their ages ranged from 3 to 51 years; 46 were males and 63 females. Of this total, 95 patients had only one type of wart (88 with common and 7 with plane warts), situated mainly on hands and limbs, including many which were periungual or palmar, and totalling 1016 lesions. Of the remaining patients, 12 had only plantar warts, with a total of 22 lesions, and two had both common and plantar warts, with a total of 14 common and 7 plantar lesions. No attempt has been made to subdivide further the types of lesions treated, as apart from these categories there was no obvious difference in response.

Table I.—*Common and Plane Warts.*

Total patients.	Cleared with single treatment.	Cleared with two treatments.	Cleared with three treatments.	Failed to respond to three treatments.	Treated by other methods after first treatment.
97	67	16	2	2	10
Total warts.					
1030	841	151	9	6	23

The results of treating common and plane warts are shown in Table I. It will be seen that with warts of these types, 67 out of 97 patients (69%) had a complete response to a single application, and 83 patients (85%) to two applications. Further, of the total number of warts in all 97 patients, 841 out of 1030 were removed with one treatment (82%). With two treatments, 992 warts were cleared (96%).

Of the 14 patients with a total of 29 plantar warts, with or without warts elsewhere, 10 patients, with 19 lesions, responded to a single application. The remaining 4 patients, with 10 warts, were all treated, after an unsuccessful initial application, by other methods. Successful results in plantar warts were thus obtained in 70% of patients treated, and in 65% of individual warts. On the basis of the response of individual warts to this therapy the results are disappointing.

The rate of recurrence in common and plane warts after apparently successful treatment, assessed in terms of numbers of patients over a period of three months, was not greater than the rate obtaining during the same period with similar cases treated by curettage in this clinic during 1950. There were recurrences in 15 out of 101 patients followed for this length of time after treatment with liquid nitrogen (15%), compared with 48 known recurrences within three months in 270 patients treated by curettage (18%) in 1950.

Conclusions.

In the treatment of common and plane warts a reasonably high percentage of success was obtained with the method. The response of plantar warts was unreliable and inferior to that from other methods.

The assessment of any treatment for warts is difficult, since it is impossible to decide to what extent suggestion plays a part. Although the results of treatment with liquid nitrogen are slightly inferior to those obtained with curettage, the former is far quicker and is therefore of special value in the treatment of patients with multiple lesions, and in young children. Scarring is negligible and sepsis rare, and as a method of radical removal of warts there appears to be no serious disadvantage attending its use. Its ready availability in most areas at the present time and its non-inflammable nature dispose of the principal general objections to the use of liquid gases.

I am indebted to Dr. J. T. Ingram, Dr. F. F. Hellier and Dr. S. T. Anning for permission to treat their cases, and for much helpful advice and encouragement in the preparation of this paper.

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JOHN MACHIN, MATHEMATICIAN AND ASTRONOMER, AND THE FIRST DESCRIPTION OF ICHTHYOSIS HYSTRIX.*

W. R. BETT.

JOHN MACHIN, who died two hundred years ago this very month, belongs to that small but fascinating band of lay clinicians who have enriched our profession with original and strikingly phrased descriptions of new diseases. We know little about him and wish we knew more. We do not even know the year of his birth. A distinguished mathematician and astronomer, he was elected a Fellow of the Royal Society in 1710, serving as Secretary from 1718 to 1747. He was Professor of Astronomy at Gresham College from 1713 until his death. In 1706 he computed the value of π by Halley's method to one hundred places of decimals.

How did it happen that a mathematician-astronomer came to describe for the first time that rare and puzzling condition "Distempered Skin," which we now call Ichthyosis hystrix? In March 1731 a country labourer from Euston Hall, Suffolk, brought his son aged fourteen to the Royal Society of London for advice, showing him at one of its meetings, and Machin, the secretary, reported a "cuticular Distemper of a different Kind from any hitherto mentioned in the Histories of Diseases" in the *Philosophical Transactions of the Royal Society* (1731, **37**, 299–301). He described the patient's skin ("if it might so be called") except on the face, palms, and soles as being like a dusky coloured bark or hide, reminiscent of a seal or rhinoceros skin or hide of an elephant. Callous and insensible, it did not bleed when cut. The bristly parts looked and rustled like the quills of a hedgehog. The skin, which was three-quarters of an inch thick, was shed every autumn without causing discomfort. "Notwithstanding the unusual disposition of his Humours to form so strange an Integument, his natural Excretions were said to be in the ordinary Course and Manner, without any thing remarkable attending them." The boy's father could not account for the condition by any accident, and the mother had had no fright while pregnant. The skin had been normal at birth; after seven or eight weeks it began to turn yellow, "as if he had had the jaundice," and then black, and later to thicken. None of the brothers or sisters were similarly afflicted. Machin's account, which

* Read at the Annual Meeting of the British Association of Dermatology at Oxford on 28 June 1951.

is illustrated by a striking folding-plate, was supplemented a quarter of a century later by Henry Barker, F.R.S., who in a paper published in the *Philosophical Transactions* (1755, **49**, 21–4) refers to this patient, Edward Lambert, being exhibited in London as the "Porcupine-man." He had had six children, five of whom had died; all were similarly affected. Like his father the surviving child also had had smallpox, when he, too, had been temporarily free from his skin disease. Barker expressed the opinion that a new race of people might be propagated by this man, "and, if this should happen, and the accidental original be forgotten, 'tis not improbable they might be deemed a different species of mankind."

Lambert's grandsons fell into the hands of a speculator named Joanny, who exhibited them on the Continent of Europe. In 1820 Francis Lambert was shown at Laxton's Rooms, 23, New Bond Street, London, being described in his bill as a new species of man: "Among the Wonders of Nature, which have from time to time tempted the Curiosity of the Public, perhaps no object more worthy of attention has been offered to their notice than a Singular Variety of the Human Species, now exhibiting." His great-grandfather's biography was considerably embellished, for he was said to have been a scaly savage from Davis Strait, taken to Philadelphia by travellers, and Pettigrew further enriched the story in his account of a "biped armadillo" (*Lancet*, 1833, **2**, 146-7).

The literature of Ichthyosis hystrix was reviewed in 1930 (*Arch. Derm. Syph., Chicago*, **22**, 307–17) by J. McFarland, who followed up the Lambert family, tracing ten cases in four generations, all being males.

ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. W. N. Goldsmith.

19 April 1951.

Chronic Disseminated Lupus Erythematosus with Lichenoid Lesions.—Dr. Benjamin Schwartz.

Mr. F. T—, aged 63, who had had no previous skin disease, first came under treatment in 1941 for undoubted chronic lupus erythematosus on the left side of the face. Between then and 1950 he was treated with carbon dioxide snow, quinine, sulphonamides, arsenic, bismuth and gold. Three separate courses of gold were given (a total of approximately 2·5 g.). There was, however, a gradual spread of the condition to the buccal mucosa, lips and scalp.

In June 1950 a new eruption appeared rapidly in two to four days, involving the arms and legs, which hitherto had not been affected by the disease. Beyond some mental anxiety the new lesions caused no constitutional disturbance, nor at the start did they irritate; some irritation is reported now. Because of the sudden spread further treatment with gold was commenced, but this, the patient states, produced more new lesions every week. The course of gold was stopped after eight injections, and he was transferred to St. George's Hospital for possible cortisone or ACTH treatment under Dr. Stephen Gold. His admission there was precipitated by the occurrence of a haemorrhagic pleural effusion. Routine investigations indicated that there was no systemic involvement with lupus erythematosus.

Present Condition.—(1) Scarred lesions of lupus erythematosus on face, lips and scalp (Fig. 1).

(2) Irregular verrucous plaques with firmly adherent scales resembling lichen planus hypertrophicus scattered over the body but chiefly involving the backs of both hands and forearms (Fig. 2), the left leg and the scalp. There was a lesion unmodified by treatment on the left thigh.

Fig. 1.

Fig. 2.

(3) A generalized slaty-grey pigmentation on a sallow skin is most noticeable on exposed areas; it is seen especially on the neck and ears where, following confinement to bed for the past three months, the distinction between exposed and unexposed areas is probably more marked than is natural.

(4) Localized lesions have markedly hyperpigmented edges.

(5) A small bullous lesion developed on the left index finger four days ago. This is the first such lesion which has occurred throughout the history of the disease.

Investigations.—W.R. and Kahn reaction, negative. Blood count, E.S.R., E.C.G., normal. Serum: total protein 7·5 g., albumin 3·2 g., globulin 4·3 g. per 100 c.c.

Histology of lichenoid lesion.—Considerable hyperkeratosis, follicular plugging, flattening of the dermo-epidermal junction and a diffuse and perivascular cellular infiltrate—features of chronic lupus erythematosus. (A similar conclusion was reached by Dr. Haber when he examined a section in November 1950, before the patient was transferred to St. George's.)

Treatment.—The lesions on the right forearm have been treated with carbon dioxide snow during the past month with considerable improvement. Local application of salicylic acid to the left arm has had little effect. An isolated lesion on the left arm was treated with x-rays (4 doses of 100 r), which resulted in a very great increase in pigmentation.

Comment.—The histology is somewhat doubtful. Lupus erythematosus is the most likely diagnosis, but it is difficult to distinguish the section from one of lichen planus. If this *is* lupus erythematosus, the clinical appearance of the lesions is somewhat unusual; in view of the pigmentation, the fact that he has had gold and that there was so much spread during the last course of gold, this condition may be a lichenoid gold eruption rather than lupus erythematosus. The recent occurrence of a bullous lesion is more in favour of lichen planus rather than of lupus erythematosus. I hoped to find gold in the tissues and a small piece was subjected to spectroscopic examination, but the evidence for the presence of gold was not very convincing.

Dr. G. B. Dowling: I have an identical case, a patient who presented herself two or three years ago with a reddish scar on the scalp. We could not make any diagnosis, but after a time she developed follicular horny plugging round the scar and we thought that the condition must be lupus erythematosus. She had no gold or other metallic treatment and carried that diagnosis for a long time; however, comparatively recently she developed lichen planus of the hypertrophic warty type on the forearms. The lesion in her scalp is not quite so lumpy as the scalp lesion in Dr. Schwartz's case but the change is of the same type. It is not always easy to distinguish lupus erythematosus of the scalp from lichen planus, and I would suggest that the present case has, throughout, been one of lichen planus.

The President: I have seen a case of quite typical discoid lupus erythematosus which became disseminated and systemic. The lesions gradually assumed the features characterizing the present case: great thickening of the skin and a warty surface, and, in places, discrete round warts. There were no small lesions suggestive of lichen planus. My patient had been given bismuth, and this may have been an important factor in inducing this lichen metamorphosis of the lupus erythematosus.

Dr. H. Haber: A case at St. John's Hospital diagnosed clinically as lupus erythematosus, when treated with gold developed a generalized lichenoid eruption, which both clinically and histologically showed overlapping features of lichen planus and lupus erythematosus. A few months later the patient's condition cleared, but he presented on his legs typical lichen planus which was confirmed histologically.

Dr. R. D. Moyle: I think the speaker omitted to mention a polygonal flat-topped papule just above the verrucose area on the forearm, similar in colour to lichen planus, and white pin-point lesions on the buccal mucosa. I feel quite sure that there is lichen planus on the left forearm and in the mouth.

Lupus Erythematosus.—Dr. Arthur Rook and Dr. P. J. B. Thomas.

D. W—, aged 24, first attended the Out-patient Department on 27.ii.51. He suffered from scarlet fever at the age of 8 and is said to have had anaemia at 13.

At 21 he had an appendicectomy. He has never suffered from any skin disorder. His mother has bronchitis but his father and younger brother are in good health. Two uncles and an aunt died of pulmonary tuberculosis.

In 1944 his left forearm was tattooed with an elaborate design in blue with roses in red. In January 1951 red patches suddenly appeared on both cheeks and enlarged rapidly over a period of a few weeks. At precisely the same time he noticed moderately severe irritation in the tattoo. This irritation has persisted. After about a week he noticed that the red areas in the tattoo were becoming raised and warty (Fig. 1), and they became increasingly so during the next three weeks. There

Fig. 1.—Forearm showing the warty appearance of the red areas of the tattoo. (Photograph of water-colour sketch by Miss J. M. Williams.)

has been no change in the facial or arm lesions in the last six weeks. The blue areas in the tattoo have not irritated at any time. He had no upper respiratory infection or any constitutional symptoms either immediately preceding the appearance of the skin lesions or subsequently.

On examination..—No discoverable physical abnormality in any system other than the skin. On both cheeks there are discoid patches of lupus erythematosus. In the tattoo there is no detectable change in the blue areas, but the roses are elevated and warty.

Investigations.—27.ii.51: Skiagram chest: No abnormality detected. White blood count within normal limits. E.S.R. 9 mm. in one hour (Wintrobe). W.R. negative. Patch test: 2% ammoniated mercury: very strongly positive.

Biopsy (Dr. I. W. Whimster).—*Arm* (a rose was excised): (Section 1) Severe generalized, irregular epidermal hyperplasia, subepidermal oedema and vascular dilatation and focal infiltration with lymphocytes (Fig. 2). There is much pigment in the upper layers of the dermis, which by transmitted light appears black but by incident light orange-red. This pigment is in colour identical with vermilion (red mercuric sulphide).

(Section 2) (not illustrated) Similar changes to (1) except that in the centre of the section there is no pigment and in this area there is no inflammation or hyperplasia. In the inflamed areas there is mild fibrinoid degeneration of the subepidermal connective tissue.

In both sections the inflammation and hyperplasia are compatible with the diagnosis of lupus erythematosus. Although the pigment appears to have the same distribution in the skin as the inflammatory reaction, the inflammation is not centred round the pigment particles themselves.

Face: The epidermis is flattened and there is keratotic plugging of the follicles: there is a marked lymphocytic infiltrate mainly around the skin appendages (Fig. 3).

Comment.—The technique of tattooing commonly practised in civilized communities is an introduction of pigment particles into the dermis with a special electric needle. Carbon in the form of Chinese or Indian ink is used to obtain the blue colours in the design and cinnabar (mercuric sulphide) for the red. The use of other pigments seems to be rather uncommon (Matthews, 1947). The delayed development of sensitivity to cinnabar has often been observed, an eczematous reaction limited to the red areas of the tattoo appearing after an interval of a few months or after many years. In some cases the reaction in the tattoo has appeared only after sensitivity to mercury has been accidentally induced by the application of a mercurial preparation to some other area of the skin, but in most cases it has developed

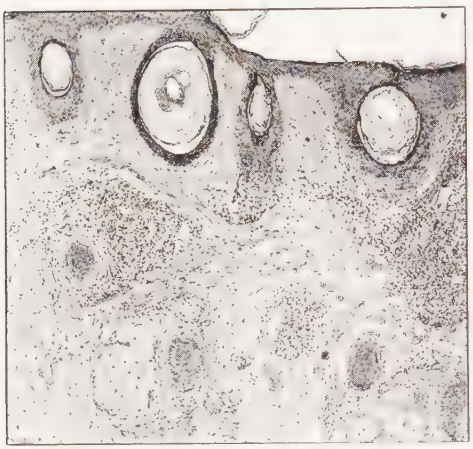

FIG. 2.

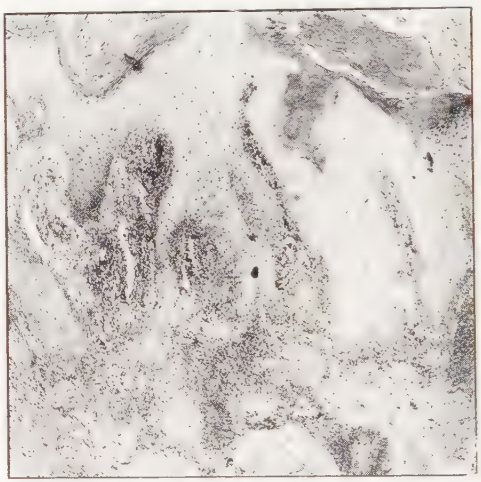

FIG. 3.

spontaneously. Usually sensitivity persists indefinitely, but Sulzberger *et al.* (1944) have reported a case in which the sensitivity diminished after a few weeks.

Madden (1949) describes a man aged 36, tattooed four years previously, who developed lupus erythematosus simultaneously on the face and in the red areas of his tattoo. On two occasions exposure of the face only to sunlight was followed by a flare of the lesions on the face and on the arm which had remained covered.

There are two possibilities to be considered. Either development of sensitivity to cinnabar is an essential pathogenic factor in provoking the lupus erythematosus reaction, or lupus erythematosus provoked by some unrelated and unknown factor localizes at the site of a pre-existing low-grade, inflammatory focus as psoriasis or lichen planus may do. However, when these latter diseases develop in tattoos, they are not localized to the red areas.

The results of patch tests with cinnabar and other mercurial compounds are inconsistent even in the simple eczematous reactions in tattoos. MacKenna (1948) has suggested that some intracellular pigment particles dissociate and form organic compounds which act as haptens.

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SULZBERGER, M. B., KANOF, A., and BAER, R. L. (1944) *U.S. Nav. med. Bull.*, **43**, 889.

Dr. A. Lyell : Had this patient used any mercurial preparation on the face before the lupus erythematosus occurred ?

Dr. A. J. Rook : The patient was not using a mercurial cream.

Dr. I. R. Marre : Two years ago I had a patient with a granulomatous eruption of the red areas of a tattoo mark on his arm. He had also a dermatitis of the beard area and it turned out that he had used a mercurial shaving cream. The granulomatous areas on the arm came up together with the eruption of the face, but the face subsided when he stopped using the mercurial cream. The granulomatous red areas of the tattoo mark were excised. He was strongly positive to mercury ointment patch tests.

Dermatomyositis in a Patient with a Past History of Carcinoma of the Ovaries.—Dr. L. Forman.

Mrs. R. S—, aged 55. Two children.

1943 : Ovaries removed with uterus for papilliferous carcinoma of ovaries.

March 1950 : Fatigue and lassitude, with stiffness of arm and trunk. This became very severe by October 1950 : was unable to dress herself and movement was very painful. At that time erythema noted on sides and back of neck, face, left ear, front of chest, shoulders and outer upper aspect of arms. Dorsal aspect of terminal phalanges became painful, erythematous, with telangiectases which were longitudinal and not punctate as in lupus erythematosus.

There is a diffuse erythema of scalp and orbits with a cyanotic tinge, and fullness of eyelids ; erythematous areas on sides of face, chin and back of neck ; a plaque on the shoulder, yellow with a slightly mamillated surface recalling pseudoxanthoma elasticum ; an erythematous patch with small areas of superficial atrophy and crusting on front of chest. The subcutaneous tissue thickened under the erythema of upper arms.

Musculature generally weak ; most easily demonstrated on elbow extension and hip flexion. No reflex or sensory changes. Sternal puncture did not reveal any Hargraves cells, nor were any seen in blister produced on skin by cantharides.

Histology (erythematous area on shoulder). Epidermis thinned to few layers of cells ; vessels of papillary and subpapillary layers of cutis dilated with slight lymphocytic surround ; connective tissue of papillary bodies and narrow band below, oedematous, and fibres form a fine reticulate pattern.

From another area, similar appearance with more oedema of epidermo-dermal junction.

Muscle biopsy from deltoid muscle—Collection of lymphocytes between the muscle bundles ; muscle fibres show oedema and longitudinal separation.

Comment.—This case is of interest because of the history of ovarian carcinoma. In my opinion the association of dermatomyositis with neoplasia is not fortuitous. It has been referred by S. Rothman (1925) *Arch. Derm. Syph., Berl.*, **149**. 99, and R. Bezecny (1935) *Arch. Derm. Syph., Berl.*, **171**. 242. Further, dermatomyositis is only one of the erythematous reactions associated with carcinoma.

The following examples have been observed personally :

(1) Man aged 65, with general muscular weakness and difficulty in swallowing. Spider naevi in large numbers on face, forehead and upper chest, with palmar erythema. Death from heart failure. At post-mortem, large gland found in mediastinum which, on section, proved to be oat-cell carcinoma.

(2) Man aged 58. Numerous spider naevi and palmar erythema. Post-mortem : carcinoma of bronchus and massive infiltration of liver.

(3) Man aged 39. Localized erythema of exposed areas of scalp, ears, face, backs of hands and chest. Areas on backs of hands hyperkeratotic and suggestive of lupus erythematosus. Clinical investigation showed no evidence of carcinoma, but blood and mucus in stools. One and three-quarter years later patient was found to have carcinoma in the abdomen.

(4) Woman aged 68. Diffuse erythema of face, scalp and limbs with telangiectasia

and superficial atrophy ; no muscle weakness : carcinoma of cervix uteri demonstrated a month after she was first seen.

(5) Characteristic dermatomyositis with erythema of face, limbs, and trunk and muscle weakness. Examples : Woman aged 60 with carcinoma of left breast. Woman aged 51 with carcinomatous glands and deposits in mediastinum ; site of primary unknown.

In the case described by Bezecny there seemed to be no doubt about the relationship between dermatomyositis and carcinoma of ovaries. Removal of the ovaries was followed by dramatic improvement in the muscle weakness within a few days. The dermatomyositis had been present a year before operation.

The relationship between the changes described and carcinoma is a matter of conjecture. Probably the skin changes are not due to toxic substances produced by the carcinoma, because two patients (5, above), showed clinical improvement of the erythema and muscle weakness although the carcinomata were progressive and inoperable. Alteration in the hormone level of the blood might explain the telangiectases and erythematous element of the reaction. Similar changes have been seen with pregnancy and in individuals with severe liver disease. One patient described (2, above) had a grossly infiltrated liver, which could quite well have given rise to changes in the blood level of oestrogens and androgens. With carcinoma of the genital organs, breasts, ovaries and uterus, significant deviations in the blood hormone level could quite well occur only during a phase in the history of the carcinoma.

Dr. S. C. Gold : There may be hormonal influence in some of these conditions. It is well known that rare cases of systemic lupus erythematosus have been improved by removal of the ovaries, yet recently I have seen two women in whom there was an undoubted association between oöphorectomy and development of lupus erythematosus. The first has since died and the second one is now in a remission stage ; it does seem that a critical balance of hormones may be an influencing factor on the development of these so-called collagenoses.

Dr. J. T. Ingram : I have recently seen at a Sheffield meeting such an erythema of the face associated with a neoplasm in the chest. Eighteen months ago Dr. F. F. Hellier had a patient with advanced dermatomyositis who is now dying from carcinomatosis though the dermatomyositis has cleared. These experiences emphasize that dermatomyositis is a symptom and not a disease. It is, however, interesting to consider the significance of the malignant reticuloses which sometimes develop from cases of poikilodermatomyositis.

There may be a close association between poikilodermia and hormonal imbalance.

Dr. R. E. Church : I am reminded of a man who was admitted to Addenbrooke's Hospital, Cambridge, with a typical attack of dermatomyositis. He had fever, oedema of the face and an erythematous rash of the face and backs of the hands similar to Dr. Forman's case. There were marked weakness and wasting of the muscles, particularly of the shoulder girdle, which progressed after the rash faded. About four months from the onset of his illness he developed a cough and abnormal signs in the chest. Skiagrams, which at the beginning of his illness showed no abnormality, now showed a carcinoma of the bronchus from which he died two months later.

Benign Familial Pemphigus (Gougerot-Hailey-Hailey).—Dr. L. Forman and Dr. H. Haber.

Mr. H. L—, aged 47.

Twenty years' history of an irritable affection of the skin of the scrotum and adjoining thighs, usually worse in the summer. During the past two years the skin of the neck has been affected at times. On examination the skin of the side of the scrotum was thickened, papilliferous, and reddened with irregular fissures. A half-moon patch of red, lightly crusted skin has been noted on the neck and scaling papules on the forehead. This patient is the brother of the woman with this disease shown at the February meeting of the section (*Brit. J. Derm.*, **63**, 459).

This patient has a widespread eruption on his forehead, ears and neck, superficially resembling a banal seborrhoeic dermatitis. He also shows angular stomatitis with leucoplakia-like lesions of the mucosa near the corners of the mouth. In the axillary folds are a few intertriginous lesions. Cytological examination of all

mentioned lesions reveals acantholytic cells typical of this condition. Histology of the lesion of the neck reveals marked acanthosis with cleft and bulla formation within the epidermis. Within the bulla many acantholytic cells are demonstrable. Changes in the upper corium are insignificant. Rubbing of normal looking skin of the trunk causes much erythema and pinpoint bleeding. Histological examination of that area revealed cracks within the epidermis indicating probably an abnormal fragility of the skin in those suffering from this dermatosis.

Adenoma Sebaceum.—Dr. C. D. Calnan (for Dr. R. T. Brain).

History.—This child, aged 6, attended hospital first in 1946 for *petit mal* epileptic attacks which began at the age of 8 months and ceased at the age of 14 months. Face eruption appeared at the age of 4 years. At the same time a tag was noticed on the left big toe-nail. Patches over lumbar area present since birth.

Family History.—No history of epilepsy. No skin lesions in family.

Mother has two normal children aged 10 and 13 by first, and one by her second husband; this patient is the only child by her third husband, one of whose brothers died (cause not known).

On examination.—Typical adenoma sebaceum of Pringle type on the face. Central part of the upper lip is spared. Fibroma at base of left big toe-nail. Band of fibrous hyperplasia over lumbar area.

Dr. Bethel Solomons: I believe that the principal future interest in adenoma sebaceum will be that of the geneticists. Any accessory factor enabling us to describe the genetics of any case is to be welcomed, and in this respect the electroencephalogram can be very helpful. Good and Garb (1943) published a paper about a family in which only one member had clinical signs of the disease and an abnormal E.E.G., whereas four of the family, although having no clinical features of the condition, had abnormal E.E.G.'s.

I think as many as possible of this patient's family should be examined by electroencephalography, in the hope that more light would be shed on the genetics of this case.

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The following case also was shown:

Pigmentary Dermatosis.—Dr. Bentley Phillips.

OXFORD REGION DERMATOLOGICAL GROUP.

President: Dr. Alice Carleton.
Meeting at Oxford on 24 February 1951.

Cases shown by Dr. Alice Carleton:

Dermatitis Artefacta.—A woman aged 31.

Two months ago this patient had a group of boils on the buttocks which cleared up with systemic penicillin.

A month ago a further boil appeared on the back of the right thigh and was treated with a kaolin poultice. The next morning there was a black eschar over the centre. She denied that she had been burnt. Local application of penicillin powder was followed by an erythema thought to be due to penicillin sensitivity.

A week later she developed a peculiar syndrome of waves of erythema spreading from the original site up the thigh, each wave consisting of a semi-lune of erythema with a sharp edge, at first dark red, and later pale red with minimal scaling. Each spread was heralded by a sensation of pain and tingling. At first the waves occurred every day, then after two weeks' interval, then after a further two weeks' interval. Then there were two more such attacks. There was no fever and general examination showed no abnormality.

In the differential diagnosis an erysipelas-like condition would have been accompanied by more disturbance. The lesion did not correspond to any of the marginate erythema group, and dermatitis artefacta was thought to be the most probable diagnosis. This was confirmed by biopsy, which showed a picture very much in favour of this, with maximal changes in the outer layers of the skin. Up to date the patient has not admitted any interference under psychiatric investigation.

Two Cases of Dermatomyositis.

Case I.—A woman aged 63.

Two years ago the patient developed redness around the fingernails with some irritation. This was succeeded by erythema of the forehead with severe irritation and loss of hair. A month later a similar rash appeared on both knuckles and spread up the lower third of both forearms, then appeared over the sternum and spread around the neck and upper half of the breasts. At this time she had a radical mastectomy followed by deep x-ray treatment. Twenty months ago red patches appeared over the elbows and definite "streaking" was seen on the metacarpals. The patient also complained of some general weakness particularly in the limbs.

Investigations.—E.S.R. 27 mm. in the first hour. Urine, 24-hour specimen: creatinine 780 mg., creatine 220 mg.

Since then there has been an improvement in the symptoms and the rash.

Case 2.—A woman aged 63.

For about two years the patient has suffered from swelling of the ankles and redness of the elbows and knees. The hands then became swollen and two months later the eyes became puffy. Red streaks appeared on the sides of the face and spread to encircle the neck. A year ago the affected areas had become deeply cyanotic and there was a deep-seated infiltration on the outer side of the left leg. A month later erythema had spread to involve the skin over the trochanter and upper part of the buttocks and ankles. There was some weakness of the legs and hips.

Investigations. Hb, 67%; White blood cells, 3700; E.S.R., 50 mm. in the first hour. Urine normal.

The following cases also were shown:

Dermatomyositis in Girl of 7; Sub-acute Disseminated Lupus Erythematosus; Striae of Adolescence Horizontal Striae on Back; Tertiary Luetic Infection Limited to One Half of Body, Previously Affected by Poliomyelitis; Morphoea; Parapsoriasis; Severe Cystic Acne; Lupus Pernio; Lichen Sclerosus et Atrophicus (2 cases; Scarring Alopecia (Naevoid); Woolly Naevus of Hair with Pigmentary Change; Urticaria Pigmentosa; Perinaevoid Vitiligo.

THE NORTH BRITISH DERMATOLOGICAL SOCIETY.

Summer Meeting, June 1951 (Aberdeen Royal Infirmary).

Lichen Planus in an Infant.—Dr. T. E. Anderson.

M. E—, a girl, aged 10 months.

History.—At the age of two weeks the child, who was breast fed at the time, developed a papulo-pustular eruption on the face, arms and legs, with some bullous lesions on the legs which ruptured and healed centrally, giving an annular appearance. This eruption resolved within four weeks on simple antiseptic preparations, but during this period some transient, rather lichenoid papulation was noted on the legs.

When the child was three months old keratodermic lesions with erythematous zones around them appeared on the dorsa of the left index and ring fingers and of the second and fourth toes of both feet.

Two weeks later a feeding difficulty occurred. Within a week of this development a generalized lichenoid eruption appeared, with classical lichen planus papules on the legs. Some of the papules on the arms were of a rather deep purplish colour and some pigmented macules were showing at the sites of involuting lesions. The mother gave no history of drug ingestion. The lesions on the trunk resolved within two weeks, but in the region of the right natal fold the Köbner phenomenon was well shown. During the following few weeks the lesions on the hands, ankles and feet became progressively more hypertrophic and verrucous. Subsequently there has been remission and relapse of the hypertrophic lesions, with the occasional accompaniment of a few ordinary lichen planus papules.

Family history.—The mother had an acute attack of lichen planus three years previously, but has noted no lesions since that date.

On examination.—On the thighs and legs are linear and reticular erythematous and pigmented marks at the sites of previous lesions, some tending to be slightly depressed (Fig. 1). About the right ankle are a few small verrucous points, and one large nodule with a markedly hyperkeratotic, verrucous summit.

Fig. 1.

General examination reveals mental retardation and some spasticity and paresis of the right arm and leg (probably from a birth trauma). There is also a marked squint due to bilateral sixth nerve paralysis.

Investigations.—Blood W. R., negative; blood count, normal; Hess's test, negative.

Histology.—(November, 1950) From thigh: Marked hyperkeratosis and slight granulosis is present; acanthosis is pronounced. Only the superficial layer of the dermis is included in the specimen and this shows no infiltrate.

Comment.—Although the biopsy unfortunately was too superficial for proper confirmation, the clinical picture is characteristic enough to make the diagnosis. The case is presented as another example of lichen planus developing in two members of the same family, but not synchronously. The long interval of freedom in the mother's case prior to the birth of the patient would rather support the evidence against an infectious aetiology for lichen planus, which Hellier (1950) reviewed.

Reference.

Hellier, F. F. (1950) *Brit. J. Derm.*, **62**, 446.

Morphoea Bullosa.—Dr. A. A. C. Ross.

Mrs. R. M—, a housewife, aged 68.

History.—She complained since about December 1947 of an itchy patch on the back which she had noted to have a purplish colour. She was referred to hospital first in April 1948, and at that time showed a band of scleroderma 10 × 6 cm. across the right lumbar region, with a lilac border and pale, alabaster-like centre; some fine points of hyperkeratosis were present towards the upper border.

In August 1948 some bullae developed over the lower part of the plaque. Healing of the bullae was slow. Since that time bullae have arisen periodically, the contents being clear, yellowish and gelatinous rather than serous: they do not rupture readily, but when they do the raw surface is painful, becomes infected readily and heals slowly.

She has had varicose veins all her adult life, and in 1950 developed static dermatitis and ulceration of the right ankle. During 1950 she also suffered from recurrent otitis externa and a few plaques of psoriasis.

On examination.—On the right lumbar region is a typical plaque of scleroderma at an inactive stage, with a place, smooth, alabaster-like appearance. No bullae are present to-day and the violaceous tint has disappeared from the border.

Investigations.—Urine: no albumen. Sulkowitch test negative. Blood urea, 30 mg. %; serum calcium, 8 mg. %. Skiagram of chest—negative. Blood-pressure, 200/100.

Histology.—(1948) The epidermis is generally thinned, with here and there loss of rete-peg formation. The dermis shows a striking thickening of the connective-tissue bundles, with hyalinisation. The whole dermis appears homogeneous and opaque, being broken only by a few distorted and displaced dermal structures, e.g., sweat glands, around which there is scanty round cell infiltration. Elastic fibres are much fragmented.

(1951) Again the picture is that of scleroderma. No myxomatous degeneration can be identified. No colour change in the collagen is demonstrable with Masson's stain, although a slight colour change is noted with van Gieson.

Comment.—This case is shown as an example of sclerodermia circumscripta pemphigoides (morphoea bullosa) discussed by Reich (1950), although unfortunately not bullous at the time of demonstration.

REFERENCE.

REICH, H. (1950) *Derm. Wschr.*, **121**, 486.

Postscript.—On the suggestion of Dr. James Sommerville the patient has since been treated with 3-hydroxy-2-phenylcinchoninic acid, with at least coincidental improvement greater than at any other time in the past three years.

Reticulosis.—Dr. T. E. ANDERSON.

J. M—, a farmer, aged 56.

History.—The illness commenced in 1945 with "itchy spots here and there" on the legs. Gradually the trunk and arms became involved. At this stage he was treated for scabies without benefit.

When seen at hospital in 1947 the appearances were those of a mild dermatitis herpetiformis with urtication of some papules and a tendency to dermographism: pigmentation was present at the sites of some resolved lesions. Many teeth were carious. The pruritus and intensity of the eruption fluctuated, the dominating feature being small wheals. By 1949 pruritus had become very marked; lichenoid papules were present with pigmented macules and maculo-papules, which urticated on friction. Loss of sleep due to the pruritus was troublesome, and the patient felt vague general malaise and excessive fatigue. By the end of 1949 he had lost almost 2 stones (about 12 kg.) in weight. General lymphadenopathy was present. No enlargement of liver or spleen was found.

Prolonged treatment with urethane (maximum dose 6 g. per day) controlled the pruritus only during administration of the drug. A test treatment with x-ray, up to 400 r to one area, gave no benefit. The only real improvement had been obtained by treatment with "R 48" (β-naphthyl-di-2-chloroethylamine) at the suggestion of Dr Ridley.

Previous history.—Gastric operation in 1917; dyspepsia troublesome since 1946. Cerebral thrombosis in 1946.

On examination. Fairly numerous infiltrated papules and pigmented macules are present over the entire integument. The skin shows slight thickening of the texture generally, but the pigmentation is minimal and urtication is not notable. Slight enlargement of the lymph nodes is present. Some loss of weight is still obvious.

Investigations.—E.S.R. 9 mm. in the first hour.

Urine shows no albumen, sugar or abnormality in the deposit.

Blood count: Eosinophilia 14%; slight hypochromia but otherwise normal.

Skiagram of chest: One or two calcified deposits towards the right base, but no other abnormality of the heart and lungs. There is an old healed fracture of the right seventh rib posteriorly.

Fractional test meal, normal.

Blood urea, 31 mg. %.

Histology. (May 1949) Skin: The epidermis shows an occasional horny plug, but is otherwise normal. Granuloma-like aggregates are present in the corium, some perivascular in distribution. Numerous mast cells are seen in association with these aggregates, suggesting urticaria pigmentosa.

(June 1949) Skin: Some oedema of the corium is present, but more notable is a diffuse leucocytic reaction, mainly perivascular, containing a high proportion of eosinophil polymorphonuclears and a certain number of mast cells.

Lymph node: A reactive follicular hyperplasia of non-specific character, the medulla showing fairly abundant eosinophils and mast cells.

(July 1949) Skin: A very little nondescript round-cell increase is present around some of the capillaries in the corium. The Prussian blue reaction is negative.

(December 1949) Skin: Now shows mycosis fungoides, with a pleomorphic perivascular cellular infiltrate, including many eosinophils, in the corium.

(February 1950) Skin: The picture is similar to that of December 1949, except that the intensity of the infiltrate is rather less.

(March 1950) Skin: A similar infiltrate, but in addition a considerable number of mast cells, as in an earlier biopsy.

Comment.—The periods of most intense urtication occurred, as would be expected, when mast cells were noted histologically in the infiltrate, but the pruritus was, if anything, more severe when the eosinophils predominated.

Dermatomyositis.—Dr. T. E. Anderson.

J. McD—, a boy aged 10.

History.—In December 1949 his mother noted one night that his face was red and the eyelids swollen. By next morning the colour had returned to normal, but the swelling persisted. Transient redness of the skin of the knuckles was also noted. Palpable enlargement of the cervical lymph-nodes was present. Within a week there developed joint pains, increasing muscle weakness and a bluish-red discoloration of the skin over the elbows. The progressive muscle weakness was accompanied by stiffness and some pain on attempting movements, intermittent pyrexia and tachycardia. Erythema was present over the face, hands, elbows, knees and feet. Soon he was completely disabled, flexion of the neck from the recumbent position being reduced to about 20° and raising of the trunk being impossible, although flexion of the extremities was still practicable. The pyrexial bouts were accompanied by paresis of the anal sphincter. A pellagroid episode had occurred.

Treatment with penicillin, streptomycin, aureomycin, sulphonamides, para-aminobenzoic acid, testosterone, calciferol, antihistaminics, heavy doses of vitamin E, a short course of Cortisone (500 mg. over six days) and three short courses of ACTH (the first 250 mg., the second 200 mg. and the third 100 mg.) had been accompanied by only slight subjective and objective improvement, maintained by splinting and exercise.

Previous history and family history.—Nothing of note.

On examination.—The face shows persistent oedema, especially of the eyelids and across the root of the nose, with the characteristic slightly violaceous erythema. The muscles of the trunk and extremities are grossly wasted, firm to touch but not tender. Flexion contractures of the elbows have developed, but splinting allows full extension of the knees.

Minimal streaky erythema is present on the extensor aspects of the joints of the fingers, elbows and knees, and telangiectasia over some of the interphalangeal joints. The skin is slightly glazed fixed and atrophic distally on the affected digits, giving a somewhat spindled appearance. Some slight hyperkeratosis and pigmentation is present over the extensor aspects of the forearms and wrists.

The patient is still unable to sit up unaided, but can turn over on his side with slight difficulty ; he can walk slowly if holding a wheeled support. The hand grips remain feeble and incomplete. There is no enlargement of liver or spleen.

Investigations. Urine : no albumen, sugar or acetone : no abnormalities in the deposit.

E.S.R. on admission was 10 mm. in the first hour (Westergren), but rose rapidly to 30 mm. and had fluctuated since between 20 mm. and 65 mm.

Blood culture, sterile.

Culture of a portion of muscle gave only a contaminant coagulase-negative *Staphylococcus albus.*

Urinary creatine 38·3 mg.% : following steroid hormone therapy values around 36·3 mg. were obtained.

Plasma proteins totalled 9·18 g.% (albumen 5·77, globulin 3·41) : later in the illness 7·17 g.% (albumen 4·14, globulin 3·03). 17-ketosteroid excretion remained low (values ranging from 1·51 mg. to 2·09 mg. in twenty four hours in place of the normal 4 mg., in spite of ACTH).

Blood count : Eosinophils 6%, otherwise normal.

Skiagrams of skull and chest : Normal.

Serum phosphate, 3·86 mg.% ; Serum potassium, 21·9 mg.%.

Electrocardiograms : normal.

Histology.—Skin : Some patchy round-cell infiltration of the corium, which tends to be perivascular. Slight flattening of the rete pegs.

Muscle : (*Specimen* 1). This shows areas of hyaline change with disappearance of the nuclei. Special staining, however, shows no loss of striation. No cellular infiltrate.

(*Specimen* 2). There are areas of hyaline change with loss of striation, and some degree of round-cell infiltration with a definite focal distribution. The changes are not characteristic enough for incontestable histological confirmation of the diagnosis.

Dermatomyositis.—Dr. A. A. C. Ross.

I. G—, a railway signalman, aged 36.

History.—The first symptoms, in 1948, were those of stiffness and pain in the joints, starting in the left wrist, then involving the right wrist, the terminal interphalangeal joints, the elbows and knees, the cervical and lumbar spine. This was regarded for over a year as an atypical rheumatoid arthritis, but then induration was noted in some of the muscles.

By January 1951 there was general muscular wasting, with flexion contractures of the elbows and metacarpo-phalangeal joints and hyperextension of the interphalangeal joints. Numerous tender nodules were palpable in the hamstrings of the right leg. The chest wall was practically fixed in the position of full expiration. The skin over the face, ears, neck and upper part of the chest was diffusely indurated with a smooth, pale yellow, shiny surface and tensely stretched over the underlying structures. The tips of the ears, the extensor aspects of the elbows, the dorsa of the hands and fingers and the extensor aspects of the knees showed a slightly violaceous erythema, telangiectasia and fine, atrophic wrinkling. The fingers were spindled and the wrists showed arthritic changes.

Brief compression of the right arm produced a marked Raynaud's phenomenon in the third, fourth and fifth fingers of the right hand.

Three short courses of ACTH were given between 13 February and 15 April totalling 850 mg. Towards the end of the final course a well-marked pericardial friction-rub developed, with moderate tachycardia and increase of cardiac shadow on x-ray, but no subjective distress after an initial pain across the chest. This rub persisted in varying degree until the end of May and was unaffected by treatment with streptomycin and PAS.

On examination.—The skin shows only a little residual thickening, with erythema over the extensor aspects of the elbows, but the muscular and joint condition remains essentially as described above. There is slightly less joint pain and the contractures have been lessened by physiotherapy, but the patient, although able to raise himself and to walk (with a little assistance), is still confined to bed on account of the recent pericarditic attack.

Investigations.—Weight 7 st. 7 lb. (48 kg.). E.S.R. 75 mm. in the first hour (Westergren). Blood urea, 23 mg.% ; blood uric acid, 3·40 mg.% ; blood creatinine mg.%. Plasma proteins 7·85 g.% (albumen 4·35, globulin 3·50). Blood count : mild leukopaenia. Serum calcium 9·8 mg.% ; serum phosphate 3·57 mg.% ; serum sodium 303 mg.% ; serum potassium 19·5 mg.%.

Urinary creatine excretion (1060 ml. and 1020 ml.) 35·05 mg.% and 53·1 mg.%.

Urinary 17-ketosteroids, 4·88 mg. in 24 hours and 5·1 mg. in 24 hours—a very low reading for a man of his age.

Electrocardiograms : Right ventricular hypertrophy. Skiagrams : Chest : Cardiac enlargement and prominence of the pulmonary artery segment : opacities (subcutaneous calcifications) in the axillae and chest wall.

Hands : Periarticular osteoporosis and soft tissue swelling.

Histology. Skin : Collagen sclerosis of the dermis, with scanty pericapillary round-cell infiltration. Some periarterial focal round-cell reaction in the adventitia of two of the larger arteries in the hypodermis—a true periarteritis.

Muscle : Two small foci of muscle-cell degeneration, with some scanty fibrocytic proliferation.

The following cases also were shown :

By Dr. T. E. Anderson : **Two Cases of Acrosclerosis ; Psoriasis Arthropathica ; Hydroa Vacciniforme with Pityriasis Rubra Pilaris : Mycosis Fungoides ; Poikiloderma Atrophicans Vasculare.**

By Dr. A. A. C. Ross : **Anetoderma ; Two Cases of Chronic Disseminated Lupus Erythematosus with buccal lesions ; Necrobiosis Lipoidica (non-diabetic) ; Lupus Erythematosus and Rheumatoid Arthritis ; Congenital Fragilitas Crinium with Trichorrhexis Nodosa.**

BOOK REVIEWS.

A Text-book of Treatment.*

The authors of this book, which is small by modern standards, state that much of the therapy described is based upon their own experience. Undoubtedly there is a need for a book mainly devoted to therapy, and although it is perfectly rational to include aetiology and diagnosis, since diagnosis should precede treatment, the result here has been to diminish the value of the work. Further, at least a third of the book has been devoted to "dermatologic pharmacopeia," which is based mainly upon U.S.P. XIV and N.F. IX. Much of this is elementary pharmacology, but it includes a lot of useful information about the antihistamine drugs; proprietary preparations that have stood the test of time; the antibiotics and information about ACTH and Cortisone. Sixteen pages are devoted to the principles of diagnosis, and the differential diagnosis of fifty-two common conditions is conveniently tabulated. The main part of the book deals with the classification and treatment of various skin diseases, and much useful information concerning their aetiology and clinical characteristics is concisely presented; but although this is useful for the student dermatologist, the net result is that the space devoted to treatment is often less than that found in the standard text-books.

For the busy practitioner this book would be useful for quick reference, and the senior dermatologist would find much of interest in what is described as the "dermatologic pharmacopeia."

It will be gathered that the title is somewhat misleading, and that the book might better be regarded as a concise treatise of the common dermatological disorders, with special emphasis on their treatment. R. T. B.

Dermatological Investigations.†

This collection of original papers on experimental dermatology, some already published the others not, is arranged in three sections, each with an introductory chapter (also translated into English) stating the relevant problems.

With advances in biochemical knowledge and technique the ideas put forward by Bloch on melanin and its formation have had to be modified. The main function of melanin in lower animals is not that of protecting the body from excessive U.V.R., and in man the pigment does not appear until some days after the skin has been exposed to U.V.R., so it cannot protect the body from being over-stimulated in the first instance. The abundance of pigment in the areolae mammae, genitals and central nervous system has to be accounted for.

There are many substances in the body that can be oxidized to melanin, and a number of enzymes, accelerators and inhibitors that have to be considered in such a process. After all, several amino-acids have a chemical structure akin to that of

* *Therapy of Dermatologic Disorders. Including a Guide to Diagnosis and a Dermatologic Pharmacopeia.* By Samuel M. Peck and George Klein. London: Henry Kimpton. Pp. 383. Price 46*s*.

†*Investigation Dermatologica.* By Marcial I. Quiroga, Carlos F. Guillot, Rodolfo N. Corti, and Eugenio Follmann. Buenos Aires: El Ateneo, 1951. Pp. 146.

tyrosine, and disturbances in tyrosine metabolism are not always accompanied by alteration in the colour of the skin, as for example tyrosinuria and alkaptonuria Although an increase of pigmentation usually follows irradiation, an excessive dose of U.V.R. is sometimes followed by depigmentation.

In 6 patients with vitiligo, tyrosinase derived from *Actinomyces chromogenus*, whether injected intracutaneously or applied in penetrosol to the patches, failed to make pigment appear, and furthermore, nodules developed at the sites of injection. The amount of copper in whole blood taken from normal and vitiliginous persons was approximately the same. Blister fluid from achromic areas did not depigment normal skin, and similar fluid from normal skin did not initiate pigment in vitiliginous patches; these results make the authors think that, compared with the action of the central nervous system, local factors are of minor importance in the aetiology of vitiligo. The amount of histamine in the pigmented and depigmented areas of those with vitiligo does not differ from that in normal subjects.

Dopa, dopa + hydroquinone, dopa + hydrogen peroxide, dopa + ascorbic acid and dopa + peroxide + ascorbic acid were injected into depigmented patches of 10 subjects which were then irradiated with U.V.R. Up to 6 months later spotty pigment had appeared in 7 patients, the best result following one injection of dopa + hydroquinone.

As injections of oxidized dopa provoked a foreign body granuloma, the various stages of evolution were studied histologically, from which the authors think that physiological participation of dopa in melanogenesis is somewhat doubtful.

Whereas plants grow new structures for new functions, animals make physiological rather than anatomical adjustments to meet the situation, metabolic changes being effected through the blood stream, the nervous system, and more locally by enzymes. Dynamic biochemistry will facilitate investigative dermatology.

The histamine content of normal skin has been estimated, and it has been confirmed that freezing with ethyl chloride for local anaesthesia lessens the amount of histamine in the skin. Sites of experimental eczema showed increased amounts of histamine compared with normal areas in the same subject.

The lipase activity in the various types of leprous skin does not differ appreciably from normal. Alkaline phosphatase is more concentrated in the pilosebaceous follicles than in the surrounding connective tissue.

Cutaneous disturbances may alter the respiratory quotient, and a rise or fall in the metabolic rate can be estimated by Warburg's method. Oxygen consumption is increased in areas of experimental eczema: the authors associate it with the rise in histamine, which, they say, is probably responsible for the increase. Administration of thyroglobulin has also been shown to accelerate the metabolism of the skin. In eczematous patients on Kempner's diet, clinical improvement ran parallel with a fall of local metabolic activity to normal.

The intermediate metabolism of the various 17-ketosteroids is not fully known. The experimenters set out to study excretory variations in various dermatoses and to seek the connection between the pituitary suprarenal mechanism and the skin. Both men and women with acne have greatly increased excretion of dehydroisoandrosterone. In eczematous women with premenstrual tension and eczema, the androgenic 17-ketosteroids were more or less normal but fell when the eczema became exacerbated.

Each paper has brief summaries in English, French and German, and article mentioned in the text are given in a list of references at the end of each paper. Those with an interest in experimental dermatology will find some stimulation in this well printed book. G. W. B.

CURRENT LITERATURE.

IS THERE AN EXUDATIVE-CELLULAR ANTAGONISM? PRELIMINARY NOTE. S. Bloquiaux. (1951) *Arch. belg. Derm. Syph.*, **7**, 34.

The author believes there is an antagonism between the exudative allergic dermatoses and cutaneous neoplasms. He points out the absence of allergic history in cancer patients; anti-allergic treatment by carcinogens, such as tar, arsenic or cellular stimulants, such as folic acid and vitamin B_{12} and conversely the anti-cancerous action of substances producing exudation such as mustard gas, urethane, colchicine, etc.; contrary modifications of serum sodium and potassium in infections and cancers, and the difficulty of producing hypersensitiveness in cancer-prone types of animals. J. K.

THE ROLE OF FOLIC ACID AND VITAMIN B_{12} IN THE TREATMENT OF HUMORAL ALLERGY. S. Bloquiaux. (1951) *Arch. belg. Derm. Syph.*, **7**, 39.

The author recalls two facts related to the exudative-cellular antagonism mentioned in the previous abstract. These are the leucopenia found in anaphylactic crises, and the suppression of asthma during acute infections accompanied by intense cellular reaction. He therefore treated 44 patients suffering from humoral allergy with the cellular stimulants folic acid and vitamin B_{12}. Encouraging results were obtained in prurigo, urticaria, pruritus ani and vulvae and eczema. Poorest results were obtained in young children. J. K.

DERMATITIS FROM LOCAL ANAESTHETICS. C. G. Lane and R. Leikart. (1951) *J. Amer. med. Ass.*, **146**, 717.

This is a complete review of the 107 published cases of epidermal supersensitivity to local anaesthetics. The number of cases reported gives no indication of the frequency of this condition, which is an important occupational risk in the dental profession. Cross-sensitivity may be wide. There is little justification for prescribing local anaesthetics for pruritic skin diseases. D. M. Pillsbury, in the discussion which follows this paper, points out that the evidence that these preparations do in fact relieve itching when they are applied to the unbroken skin is extremely dubious. A. J. R.

DEVELOPMENT OF TOLERANCE OF SKIN TOWARDS ANTI-HISTAMINIC DRUGS. Samuel Monash. (1950) *Urol. cutan. Rev.*, **54**, 722.

Threshold skin reactions to histamine phosphate introduced by iontophoresis vary over a wide range in different persons, and in the same person at different times. Significant raising of threshold was demonstrated after feeding 100 mg. Benadryl, and 8 mg. of chlortrimeton maleate. But similar and greater doses given at intervals of a few days showed a diminishing effect in raising the threshold until finally double the normal dose produced no effect. The experiments were carried out by the author on himself, and confirmed by repetition on his wife and in 8 out of 9 other volunteers. Pyribenzamine and Thephorin produced a similar refractory response. C. H. W.

CHLORIDERMA (PRELIMINARY REPORT). Cleveland J. White. (1951) *Urol. cutan. Rev.*, **55**, 165.

Seven patients were observed suffering from acneiform eruptions on the face which were traced to high intake of chlorides, with high levels of blood chlorides. Restriction of chloride intake cured the lesions, relapse following when the chlorides were again increased. Medicines, certain salt substitutes and some "preserved" foods are likely unsuspected sources. C. H. W.

TAR THERAPY IN THE EARLY STAGE OF ECZEMA. H. Friderich and R. Schmitz. (1951) *Derm. Wschr.*, **123**, 409.

Tar was recommended for skin diseases 2000 years ago by Dioscorides. In the authors' opinion reactions to tar preparations are more often due to the base than to the tar. In the treatment of eczema they recommend pure coal tar, even in the acute stage. They use it incorporated in Fissan oil as a rule in a strength of 2%. Seborrhoeic eczema responds well also, and even secondary infection. M. S. S.

THE TREATMENT OF LEG ULCERS WITH HIGH DOSES OF VITAMIN E. A. Wegner. (1951) *Derm. Wschr.*, **123**, 385.

Of 10 women with varicose ulcers treated with high doses of vitamin E (300 mg. daily) 3 healed astonishingly quickly, and a striking phenomenon was the increased exudation in the area after three days' treatment. This was ascribed by the author to improved vascularization and was considered a good prognostic sign. The ulcers of the remaining 6 did not appear to improve with the vitamin E, and it was found also that only when local measures and bed rest were carried out in addition to the vitamin E therapy was any improvement to be obtained. In view of the high cost of the remedy and the uncertain result (poorer with older patients) the author considers it important to be able to judge early if such treatment is justifiable. M. S. S.

ON TH. GRÜNEBERG'S WORK: ADRENAL CORTEX PREPARATIONS IN PSORIASIS. F. Fleck. (1951) *Derm. Wschr.*, **123**, 415.

The author replies to Grüneberg's article (*Derm. Wschr.*, **123**, 173) claiming to be the first to use adrenal cortical extract in psoriasis. He finds the first reference to the therapeutic use of adrenal cortical extract in the *Anat. Rec.* (*Am.*), **44**, 225 (1929), by Swingle, Pfiffner, Hartmann, Rogoff and Stewart, but does not mention whether this was used in psoriasis. He feels that Cortisone and ACTH have too many disadvantages in price, side effects and recurrences to warrant their everyday use in psoriasis as yet. M. S. S.

LACTOFLAVINE CONTENT OF SCALE CRUSTS IN PSORIASIS. B. Zorn. (1951) *Derm. Wschr.*, **123**, 457.

By using larger quantities of material than formerly the author is now able to agree with R. de Preux's finding of a surprisingly high lactoflavine content in the scale crusts of psoriasis. He considers that this is due merely to the admixture of serous exudate with the scales and that it has little significance. He describes in detail the method used in the estimation. M. S. S.

SYMPTOMATOLOGY OF PEMPHIGUS JUVENILIS. F. Sprenger. (1951) *Derm. Wschr.*, **123**, 459.

The author describes as pemphigus juvenilis a bullous (or medallion-like) eruption on trunk, limbs and scalp, oral mucous membrane and tympanic membranes in a child aged 9½. The tympanic membrane lesions, herpes simplex-like in appearance, healed within 3 days. The ears were painful the first day. Many milium bodies, especially on the scalp, accompanied the healing of lesions. The disease ran a benign course, favouring a diagnosis of *D. herpetiformis*, but against such a diagnosis the author considers the absence of grouping of the lesions, absence of itch, involvement of mucous membrane of mouth, negative KI test, etc. The blood and blister serum showed an eosinophilia. Nikolsky's sign was absent. Neither parenteral penicillin, aureomycin nor neo-uliron influenced the eruption. No mention is made of the use of arsenic or sulphapyridine. M. S. S.

NITROGEN MUSTARD TREATMENT OF MYCOSIS FUNGOIDES. W. Bertlich and H. J. Herte. (1951) *Derm. Wschr.*, **123**, 481.

The authors prefer local x-ray treatment of mycosis fungoides in the tumour stage to nitrogen mustard therapy owing to the severe side effects of the latter. Following radiotherapy there may be remissions lasting months or years, and it may be many years before harmful effects of repeated applications show themselves. They compare the histological findings in the same area before and just after completion of the two types of treatment. The histological result was (with one exception) less satisfactory with nitrogen mustard, much more of the recognizable cell structure remaining, while with x-ray treatment this tends to be obliterated by fibrosis with only a few cell nests remaining. In all nine patients were investigated. All received nitrogen mustard and three later received x-ray therapy.

Many microphotographs accompany the text. M. S. S.

CLINICAL EXPERIENCES WITH ANTIHISTAMINE SALVE. O. Braun. (1951) *Derm. Wschr.*, **123**, 535.

The author seeks to prove that antihistamines applied locally are antipruritic owing to their anaesthetic effect. Experimentally he found that pruritus disappeared in an affected area simultaneously with diminution of touch sensation in a control patch of sound skin. He stresses the importance of its use locally in light sensitivity owing to its absorptive action in relation to ultra-

violet light. He combines with it P.A.S., which has a similar action. Any sensitivity reaction to a local antihistamine preparation is doubtless due to the vehicle employed and not to the antihistamine itself. With the use of pyribenzamine in several hundred cases the author has encountered no sensitivity reaction. M. S. S.

SUCCESSFUL TREATMENT OF LUPUS ERYTHEMATOSUS WITH ACUTE EXACERBATION WITH PENICILLIN. H. Götz. (1951) *Derm. Wschr.*, **123**, 553.

An acute grave exacerbation with dissemination of a discoid lupus erythematosus yielded to treatment with penicillin and calcium-antistin solution, both given twice daily by injection. A total of 10 million units of penicillin was given, yet during treatment acute otitis media developed. This responded to aristamid drops and aristamid oral medication. On discharge 8 weeks after admission even the discoid lesions had healed, leaving only faint pigmentation. The author attributes this very satisfactory response to the prolonged pyrexia and penicillin. He is accustomed to using pyrifer combined with pencillin in the treatment of discoid lupus erythematosus, giving injections of the pyrifer every second day in increasing concentration until 10 febrile peaks have been obtained, and the depot penicillin in doses of 300,000 O.u. daily. M. S. S.

CHANGES IN REGIONAL LYMPH NODES IN TULARAEMIA. H. Reich. (1951) *Arch. Derm. Syph., Berl.*, **192**, 175.

Small epidemics of tularaemia have recently been reported from France and Germany. Lymphadenitis of the regional glands draining the area of the primary skin or mucous membrane complex is the most prominent clinical feature. Differential diagnosis, especially from tuberculosis, presents difficulty. Some of the distinctive features of tularaemia in the lymph nodes are : (1) Specific changes occur in small foci, well separated from each other, and in these three zones, central, intermediate and peripheral, can be recognized. (2) The necrobiotic change is less uniform than the central necrosis of tuberculous caseation ; nuclear remains, lymphocytes and erythrocytes are numerous. (3) An inflammatory, hyperaemic, haemorrhagic peripheral region is conspicuous. (4) The rapid formation of a vascular granulation tissue soon replaces the specific picture. M. F.

CLINICAL FEATURES AND PATHOGENESIS OF HYALINOSIS CUTIS ET MUCOSAE (LIPOID-PROTEINOSIS OF URBACH-WIETHE). K. H. Holtz and W. Schulze. (1951) *Arch. Derm. Syph., Berl.*, **192**, 206.

Three patients are described in detail. It is likely that the disease is inherited as a recessive characteristic. Protein metabolism rather than lipoid metabolism appears to be at fault. M. F.

FINE STRUCTURE OF SOFT TISSUES AS SHOWN IN X-RAY. H. Schuermann and G. Bonse. (1951) *Arch. Derm. Syph., Berl.*, **192**, 238.

A technique is described and illustrated by the findings, under x-ray, in acrodermatitis chronica atrophicans, progressive diffuse sclerodermia and acute systemic lupus erythematosus. M. F.

ECZEMA : A PSYCHOSOMATIC STUDY. Eric Wittkower and Peter G. Edgell. (1951) *Arch. Derm. Syph., Chicago*, **63**, 207.

This article, based on an elaborate investigation of 90 patients suffering from endogenous eczema and 50 controls, shows that an hereditary predisposition to eczema and asthma existed in the group of patients studied, that specific mental situations precipitated attacks, and that among " childhood " eczema patients there was a high incidence of " difficult " positions in the family. Patients as a whole tended to have been either " unwanted " or " spoiled " children. J. K.

ESTROGENS BY LOCAL APPLICATION IN TREATMENT OF ACNE VULGARIS. Irving Shapiro. (1951) *Arch. Derm. Syph., Chicago*, **63**, 224.

The author obtained rapid results in 15 of 25 patients with acne vulgaris resistant to usual therapeutic measures with local injunction of a cream containing 2·5 mg. water-soluble conjugated oestrogens (equine) per gramme. In 7 other patients the results were less prompt. No harmful effect was noted after 4–6 months' treatment. J. K.

PROGESTERONE THERAPY IN DERMATOSES OF PREGNANCY (HERPES GESTATIONIS). Corinn Keatz, Phyllis E. Jones and John H. Lamb. (1951) *Arch. Derm. Syph., Chicago*, **63**, 675.

The authors treated 10 cases of herpes gestationis with progesterone, 20 to 25 mg. daily, with remission of symptoms and foetal survival in each instance : 4 patients had had skin lesions with previous pregnancies, one three times and one twice. Out of 20 previous pregnancies 6 had proved fatal to the foetus ; it would appear that 3 had occurred with the same patient, each time accompanied by the dermatosis, but the other 3 were unaccompanied by material skin eruption ; the relative table, however, is inaccurate. In 7 of the patients blood level of chorionic gonadotropic hormone was abnormally high. J. K.

PLASMA PROTEINS IN VARIOUS DISEASES OF THE SKIN : ELECTROPHORETIC STUDIES. Walter F. Lever, Ethel L. Schultz and Nancy A. Hurley. (1951) *Arch. Derm. Syph., Chicago*, **63**, 702.

This article, some 27 pages long, deserves reading in full. It reviews the literature and details the authors' findings in the investigation of numerous dermatoses. They conclude that though significant changes were found in the electrophoretic pattern in many diseases of the skin, these are of no diagnostic value but reflect the patient's reaction to his disease. J. K.

TREATMENT OF CHRONIC CUTANEOUS PROBLEMS WITH CALCIFEROL. Lawrence C. Goldberg and Helen L. T. Dexter. (1951) *Arch. Derm. Syph., Chicago*, **63**, 729.

Although the authors found no improvement with large doses of calciferol (150,000 i.u. daily for an adult) in cases of chronic eczematoid dermatitis, psoriasis, acne conglobata, chronic discoid lupus erythematosus, granuloma annulare, mycosis fungoides and parapsoriasis, they get favourable results in atopic dermatitis even of long standing. J. K.

LICHEN SIMPLEX CHRONICUS (VIDAL) TREATED SUCCESSFULLY WITH PODOPHYLLIN. John Garb. (1951) *Arch. Derm. Syph., Chicago*, **63**, 740.

The author treated 7 cases of lichen simplex chronicus with weekly applications of podophyllin in alcohol or ointment in strengths of 1 to 25% with considerable reaction but with success in 5 cases. The usual application used was 1–2% podophyllin in ointment. J. K.

NOTES ON CUTANEOUS REACTIONS IN BENIGN LYMPHOGRANULOMATOSIS (BESNIER-BOECK-SCHAUMANN DISEASE). A. Dupont. (1951) *Arch. belg. Derm. Syph.*, **7**, 104.

The author used Kveim antigen in testing two patients, one who had Schaumann's disease and one with tuberculosis. There was no reaction in the latter, but a positive reaction in the former showed on biopsy a sarcoid structure histologically. Intradermal injections of tuberculin were then made in 3 cases, 1 of Schaumann's disease, 1 of dormant tuberculosis and 1 of silicosis. The reaction in the first case was clinically negative, but a biopsy of the injection site made 16 days later showed histological evidence of sarcoid structure, whereas the two latter patients had a positive reaction, but biopsies made over three weeks and six weeks later respectively showed only very banal histological changes. J. K.

EXPERIMENTAL INVESTIGATIONS ON THALLIUM POISONING IN THE RAT. N. Thyresson. (1951) *Acta derm.—venereol., Stockh.*, **31**, 3.

Thallium metabolism in rats was investigated by using radioactive thallium in experimental acute and chronic poisoning conditions. Thallium causes alopecia by disturbing the formation of keratin in the hair-follicles ; excess of cystine may counteract this effect. G. A. H.

SCHAMBERG'S DISEASE WITH KERATOSES. J. N. Jorgen. (1951) *Acta derm.-venereol., Stockh.*, **31**, 28.

A patient, when aged 15, had a dry rough skin on the palms of both hands, which later developed into keratosis. Twenty years later he developed an unusual reddish-brown macular eruption, which on the legs later became darker and exhibited the picture of Schamberg's disease. Biopsy showed subepithelial inflammation with deposition of a brown pigment in the cells giving an iron reaction. G. A. H.

THE PATHOGENESIS OF ALLERGIC ECZEMA, ILLUSTRATED BY TRANSPLANTATION EXPERIMENTS. H. Haxthausen, (1951) *Acta derm.—venereol., Stockh.*, **31**, 42.

It used to be assumed that sensitivity must be due either to a permanent alteration of the ability to react in the cells themselves or to antibodies which are firmly and intimately connected with them. Transplantation experiments however show that the eczematous allergic reaction is not a stationary condition, and normal skin temporary healed in a sensitive individual acquires in a few days its sensitivity, which suggests that the allergic person constantly produces a factor which makes it sensitive by penetrating the skin. On the other hand sensitive skin after transplantation loses its power to react. Some factor from within the person is decisive in the eczematous allergic sensitivity. Recent experiments of the author suggest that it is connected with the lymphocytes. G. A. H.

BACITRACIN IN DERMATOLOGY: ITS EFFECTIVENESS IN TOPICAL THERAPY. E. F. Finnerty. (1951) *New Engl. J. Med.*, **245**, 14.

Bacitracin, either as an ointment containing 500 units per g. of petrolatum, or as a lotion containing the same number of units per c.c., was used to treat 83 cases, 75 of them being pyodermas: 61% were cured and 30% improved. Sensitization was noted in two cases only. Bacitracin was found to be effective in many cases in which the organism was resistant to penicillin, and this quality, allied to its small tendency to produce sensitization, makes it very suitable for topical therapy. A. D. P.

THE CUTANEOUS TOXICITY AND THERAPEUTIC EFFECTIVENESS OF PENICILLIN O. R. A. Marsh and J. G. Tillotson. (1951) *New Engl. J. Med.*, **245**, 17.

Penicillin O was an effective antibiotic in 52 patients suffering from a wide variety of disorders. Maculo-papular eruptions appeared in four, two of whom had previously shown sensitivity to penicillin G. Other cases, however, known to be sensitive to penicillin G tolerated penicillin O. A. D. P.

DISCUSSION ON VARIOUS FORMS OF PRIMARY CUTANEOUS DIPHTHERIA. P. Le Coulant and Sourreil. (1951) *Ann. Derm. Syph.*, **78**, 300.

The authors describe and illustrate five cases of primary cutaneous diphtheria, presenting respectively as retro-auricular intertrigo, impetigo, haemorrhagic and crusting ulcerations, and two with a varicelliform eruption. They stress that with careful observation diagnosis should be made before laboratory results are back. The characteristic diagnostic features are sanious varicelliform pustules, the erosive character of the lesions, the sero-haemorrhagic crusts, the sero-fibrinoid greyish plaques, the oedema and general signs. F. F. H.

THREE CASES OF OSTEO-HYPERTROPHIC VARICOSE NAEVUS OF KLIPPEL-TRENAUNAY. C. A. Van der Harst. (1951) *Ann. Derm. Syph.*, **78**, 315.

Three typical cases are described and well illustrated, with in one case that of a skiagram. In one patient a marked difference in blood pressure between the two arms suggested an arterio-venous communication. F. F. H.

IS PSORIASIS A PSYCHO-DERMATOSIS? M. Bolgert, R. Poisson and M. Soulé. (1951) *Ann. Derm. Syph.*, **78**, 273.

The authors believe that psoriasis is not only occasionally precipitated by nervous causes but that these are the essential cause. They investigated 33 patients: in 78·78 per cent (*sic!*) of these they found a correlation between psychic shocks and the attacks of the psoriasis. They believe that all patients should be treated along psychiatric lines. F. F. H.

DYSHIDROSIFORM DERMATITIS OF THE HANDS AND FEET CAUSED BY ASPERGILLUS. X. Vilanova and M. Casanovas. (1951) *Ann. Derm. Syph.*, **78**, 292.

A doctor presented pompholyx-like lesions that resisted all the usual treatments and from which an aspergillus was rapidly grown. The condition cleared rapidly on giving potassium iodide by mouth. The fungus was found to be related to *Aspergillus ustus*. F. F. H.

PENICILLIN: ITS ACTION AND ACCIDENTS IN THE TREATMENT OF SYPHILIS. P. Photinos. (1951) *Ann. Derm. Syph.*, **78**, 297.

Spirochaetes were found to disappear in three hours from local lesions after an injection of 100,000 units of penicillin. Higher doses did not show any greater activity. Three serious incidents are reported following penicillin, in one of which the patient died with erythroderma and oedema. F. F. H.

DERMATITIS FROM METHANOL. H. Chatard and E. Gimbert. (1951) *Arch. des Mal. profess.*, **12**, 436.

Dermatitis affected 25% of employees in a workshop where methanol was handled and patch tests with this substance were strongly positive. Preventive measures, including barrier creams and rubber gloves, did not enable men to return to work with impunity. Despite this these men were not entitled to compensation under the French law, and the authors discuss the legal aspects of the anomalous position thus arising. F. F. H.

VITILIGO WITH RAISED BORDERS. M. I. Quiroga, E. Follman and J. Chiriboga. (1950) *Rev. argent. dermatosif.*, **34**, 281.

A man, aged 30, had been seen two years before with a number of depigmented areas resembling vitiligo except that some of the lesions had an erythematous raised rim, 1–2 mm. wide, which histologically showed a subacute non-specific inflammatory reaction. According to the patient the lesions began as rose-coloured macules, which increased in size, leaving the inner part depigmented. There was no itching or change in sensation. All examinations to find a cause were negative. When seen again 16 months later the red margin has disappeared and the clinical appearance was that of vitiligo.

The authors discuss this uncommon condition and say that such cases fall into three groups —those due to pinta, syphilis and the remainder to which no cause can be assigned. G. W. B.

COLLOIDOSIS CIRCUMSCRIPTA. M. I. Quiroga and E. Follman. (1950) *Rev. argent. dermatosif.*, **34**, 206.

On the face of a woman, aged 21, were 5 lesions, from 1·5 to 4 cm. in diameter, that had arisen without obvious cause or symptoms in the last two years. All were sharply demarcated from the surrounding skin, above which they were raised about 2 mm. They were dark brown in colour and the surfaces were irregular and in places lobulated. Follicular orifices were enlarged, and the epithelium was otherwise normal. The lesions felt soft and myxomatous. Histology: The epidermis was slightly thinned and the dermal border was almost a straight line; sweat glands were considerably fewer than normal and sebaceous glands were rudimentary. The uppermost part of the dermis, corresponding to the papillary and subpapillary zone, appeared almost normal and contrasted sharply with the deeper part, where the cellular elements were diminished; the collagen fibres were swollen and had lost their fibrillary structure and showed both homogeneous blocks and fragmentation. Elastic fibres were absent. There was a slight perivascular and perifollicular infiltration of inflammatory cells.

In two tables the authors show the clinical and histological peculiarities of this and 7 other types of colloid dystrophy, to none of which this condition can be assigned, and so have given it the title above. G. W. B.

THERAPEUTIC ACTION OF OIL OF SAPUCAINHA IN SCABIES AND TINEA CAPITIS. R. D. Azulay, R. A. Seba and N. M. Moreira. (1951) *An. brasil. derm. sif.*, **26**, 79.

Brazilian natives used oil of sapucainha, a mixture of cylic fatty acids containing mainly hydnocarpus (45%) and chaulmoogra (24·4%) oils, for treating several skin diseases. The authors tried a preparation from this oil in scabies and tinea capitis. All the 185 cases of scabies were cured after three treatments and 25 of the 26 cases of tinea capitis were cured. Their formula was oil of sapucainha 2·5%, the benzyl esters of the above fatty acids 15%, in a cream of stearic acid, glycerine and triethanolamine. The oils do not sensitize or irritate the skin. G. W. B.

HERPES ZOSTER WITH A VARICELLIFORM ERUPTION AND PAROTITIS IN CHRONIC LEUKAEMIA. M. L. Gelfand. (1951) *J. Amer. med. Ass.*, **145**, 560.

A man, aged 70, with zoster of the ophthalmic type was treated with aureomycin ; the skin eruption, orchitis and parotitis cleared within 3 weeks, but he was left with severe keratitis and scleritis. A. J. R.

HERPANGINA. R. J. Huebner, R. M. Cole, E. A. Beeman, J. A. Bell and J. H. Peers. (1951) *J. Amer. med. Ass.*, **145**, 628.

The specific infectious disease first described by Zahorsky in 1920 as herpangina has been attributed to the herpes simplex virus although this has never been isolated. Outbreaks occurred in a suburb of Washington in the summer of 1950, and viruses of the Coxsackie group A were isolated from 32 of 37 patients. Neutralizing antibodies were found in high titre in the serum of 4 patients who were tested. The investigation to incriminate these viruses in this and other outbreaks is described in full.

Herpangina affects mainly children and is most prevalent in the summer months. After an acute febrile onset with vomiting and anorexia, minute vesicles which rapidly develop into punched-out ulcers appear on the fauces and dysphagia may be severe. Local and general symptoms clear after a few days. A. J. R.

QUINIDINE-INDUCED EXFOLIATIVE DERMATITIS. D. R. Taylor and R. Potashnick. (1951) *J. Amer. med. Ass.*, **145**, 641.

A man, aged 59, who was receiving oral quinidine sulphate developed after about 5 weeks a maculo-papular eruption. The quinidine was continued and 2 weeks later exfoliative dermatitis developed. He made a good recovery. A. J. R.

PHARMACOLOGIC AND TOXICOLOGIC ASPECTS OF D.D.T. (CHLOROPHENOTHANE U.S.P.). REPORT OF THE COMMITTEE ON PESTICIDES. (1951) *J. Amer. med. Ass.*, **145**, 728.

The different grades of D.D.T. used chemically have a variable composition. They are mixtures of the isomers of dichlorodiphenyltrichloroethane. D.D.T., although inherently toxic, is safe in powder form as it is not absorbed. Many of the reported toxic symptoms are due to impurities or to solvents. The reported cases of poisoning which are accepted as due to D.D.T. are tabulated. None has resulted from the domestic or garden use of the powder, but the solution has occasionally given rise to dermatitis. Precautions must be taken to avoid accidental ingestion of any D.D.T. preparation. A. J. R.

HYPERVITAMINOSIS : A REPORT OF A CASE IN AN ADULT. M. B. Sulzberger and M. P. Lazar. (1951) *J. Amer. med. Ass.*, **146**, 788.

Hypervitaminosis A has not previously been reported in an adult. A woman, aged 44, who had taken 600,000 units of vitamin A daily for 18 months, complained of night sweats of 6 months' duration, fissuring and soreness of the angles of the mouth and nares and shortening of the menstrual cycle for 5 months, bone and joint pains for 3 months, and generalized pruritus, dryness and desquamation of the skin, thinning of the scalp hair and loss of eyebrows, lashes, axillary, pubic and lanugo hair for 2 months. There was tenderness over the long bones on deep pressure. There were pigmentation of Riehl's melanosis-type of the sides of the face and neck, fine scaling of the back and limbs, follicular papules on the limbs and acneiform and milium-like lesions of the forehead. Within 2 weeks of stopping vitamin A many symptoms had cleared and the skin was normal except for the pigmentation. Hair fall had more or less ceased after 2 months and regrowth then commenced.

This case is important in view of the increasing frequency with which large doses of vitamin A are prescribed. The authors' comments on the case are of great interest. The relationship between vitamin A and the thyroid is discussed, and resemblances between the manifestations of hypovitaminosis A and hypervitaminosis A are pointed out. A. J. R.

BOECK'S SARCOID WITH COMPLETE HEART BLOCK MIMICKING CAROTID SINUS SYNCOPE. S. Simkins. (1951) *J. Amer. med. Ass.*, **146**, 794.

The detailed report of a case of sarcoidosis in a woman, aged 42, with massive involvement of the auriculoventricular bundle. Cardiac involvement is not exceptionally rare in sarcoidosis and increases the gravity of the prognosis. A. J. R.

ACTH AND CORTISONE IN DIFFUSE COLLAGEN DISEASE AND CHRONIC DERMATOSES. E. N. Irons, J. P. Ayer, R. G. Brown and S. H. Armstrong. (1951) *J. Amer. med. Ass.*, **145**, 861.

The effects of ACTH and Cortisone were contrasted in 13 patients with diffuse "collagen diseases" and in three other conditions. In acute disseminated lupus erythematosus ACTH induced remissions more rapidly than Cortisone, but because of the higher incidence of side effects with ACTH, remissions are best maintained on Cortisone. Cortisone in doses up to 200 mg. daily was found to be without effect in scleroderma, psoriasis and exfoliative dermatitis, in contrast with the dramatic action of ACTH. Although ACTH may be life-saving in lupus erythematosus no permanent cure was observed, and no skin biopsies have shown complete reversion to normal. A. J. R.

CONGENITAL VASCULAR ANOMALIES. A. W. Thompson and J. C. Shafter. (1951) *J. Amer. med. Ass.*, **145**, 869.

Ten cases of congenital vascular anomalies of the extremities are reported and the literature is reviewed. The clinical features of these anomalies depend on the stage of embryologic development, capillary, retiform or tubular, at which maturation ceases. The newer methods of diagnosis are described and a new and practical classification suggested. A. J. R.

CURRENT STATUS OF THERAPY IN LEPROSY. F. A. Johansen and P. T. Erickson. (1950) *J. Amer. med. Ass.*, **144**, 985.

This is a full and useful review of the subject by two authors experienced in the treatment of leprosy. The advantages and disadvantages of the newer drugs are discussed. Dihydrostreptomycin is useful in combination with the sulphones. A. J. R.

TREATMENT OF ACNE VULGARIS. G. C. Andrews, A. N. Domonkos and C. F. Post. (1951) *J. Amer. med. Ass.*, **146**, 1107.

The authors' concept of acne includes a belief that pustular, nodular and cystic cases are sensitized to the staphylococcus, and that the strains of staphylococcus differ widely in their sensitivity to various antibiotics and are usually insensitive to penicillin. The treatment of foci of infection is regarded as important.

A series of 384 cases is reported. The treatment included oestrogens, sulphadiazine, terramycin, aureomycin or other antibiotics, vitamin A if comedones were present and conventional local applications, but no x-ray. Twenty-three per cent. of the patients were cured and 71% improved. These figures were compared with the results of treatment of a series of 253 cases with x-ray therapy but without oestrogens or chemotherapy. In this control series only 60% were cured or improved. A. J. R.

TREATMENT OF PSORIASIS WITH UNDECYLENIC ACID BY MOUTH. H. Rattner and H. Rodin. (1951) *J. Amer. med. Ass.*, **146**, 1113.

A questionary on the subject of the treatment of psoriasis with undecylenic acid was sent to many leading dermatologists. The authors are consequently able to report on the treatment of 1106 cases. The great majority of dermatologists reported unfavourably and many consider the treatment worthless and dangerous. Side effects range from mild gastro-intestinal disturbances to exfoliative dermatitis, toxic labyrinthitis and nephritis. A. J. R.

BROMIDE INTOXICATION TREATED WITH AMMONIUM CHLORIDE. T. Cornbleet. (1951) *J. Amer. med. Ass.*, **146**, 1116.

In a carefully controlled study of patients with bromide eruptions and of experimental subjects, ammonium chloride was shown to produce a more rapid fall in the blood bromide level than sodium chloride. In the patients with bromide eruptions the clinical response was also more rapid. The theoretical implications of this observation are discussed. A. J. R.

ADULT FORM OF CHRONIC PORPHYRIA WITH CUTANEOUS MANIFESTATIONS. L. A. Brunsting, H. L. Mason and R. A. Aldrich. (1951) *J. Amer. med. Ass.*, **146**, 1207.

Twenty-one patients with the adult form of chronic porphyria have been seen at the Mayo Clinic over a period of 5 or 6 years. Seventeen of them are reported here. Clinically the condition begins in adult life with diffuse melanosis of exposed skin and hair. The complexion becomes

dusky and the conjunctivae injected, to give a "bleary-eyed" appearance. The skin of the eyelids is tinted pink. There is blistering of the backs of the hands and of the ears on exposure to light or trauma. There may be associated abdominal colic or nervous symptoms. The exact classification of this type of porphyria from a biochemical point of view remains unsettled, as the biochemical findings are inconstant and there may be few or no abnormal prophyrins in the urine at some stages. Liver damage is responsible for the development of clinical symptoms. In the present series of cases alcoholism was present in 12, active diabetes in 3 and syphilis in 2. In 2 cases barbiturates and in 1 case arsenic were believed to have played some part.

A. J. R.

SARCOIDOSIS DIAGNOSED BY MEANS OF SUBCLAVIAN LYMPH NODE BIOPSY. H. A. Weiss, R. M. Campbell, G. C. Budenz and C. M. McCanless. (1951) *J. Amer. med. Ass.*, **146**, 1221.

In a case of pulmonary sarcoidosis with no superficial lymphadenopathy the diagnosis was established by biopsy of a subclavian lymph gland. The surgical approach is the same as for the operation for phrenic crush. A. J. R.

PENICILLIN TREATMENT OF SYPHILIS. A. C. Curtis, D. K. Kitchen, P. A. O'Leary, H. Rattner, C. R. Rein, A. G. Schoch, L. W. Shaffer and U. J. Wile. (1951) *J. Amer. med. Ass.*, **145**, 1223.

This important summary of schedules for the treatment of the various stages of syphilis is based on the experience of many large clinics over a period of about 8 years. The authors are satisfied that the use of the heavy metals does not improve the excellent results obtainable with penicillin alone, and have therefore abandoned them. A. J. R.

SUCCESSFUL TREATMENT OF DERMATITIS DUE TO CHRYSOTHERAPY WITH ADRENOCORTICOTROPIC HORMONE. C. L. Steinberg and A. I. Roodenburg. (1951) *J. Amer. med. Ass.*, **146**, 1225.

A man, aged 41,whose rheumatoid arthritis was treated with myocrisin developed dermatitis, which responded rapidly to ACTH 15 mg. 6-hourly for 3 days, 20 mg. 6-hourly for 7 days and then gradually decreasing doses. A. J. R.

CORTISONE-TREATED SCLERODERMA. J. G. Sharnoff, H. L. Carideo and I. D. Stein. (1951) *J. Amer. med. Ass.*, **145**, 1230.

A woman, aged 41, with diffuse scleroderma involving the face, chest and extremities was treated with Cortisone. She received 300 mg. on the first day, 200 mg. on the second day and 100 mg. daily thereafter. There was a dramatic and striking reponse to this treatment, but within 10 weeks she developed irreversible hypertension and died in uraemia. At autopsy intimal fibrosis of the interlobular arteries of the kidneys was found and was considered to be part of the scleroderma. Wedge-shaped infarctions of the cortex are believed to have been the consequence of treatment. A. J. R.

ANAPHYLACTIC REACTIONS FROM LOCAL USE OF PENICILLIN. R. Everett. (1951) *J. Amer. med. Ass.*, **146**, 1314.

Two severe reactions occurred after the nasal instillation of penicillin in patients who had previously received penicillin on many occasions. A. J. R.

CYTOLOGIC SMEARS IN DIAGNOSIS OF HERPES SIMPLEX, HERPES ZOSTER AND VARICELLA. H. Blank, C. F. Burgoon, G. D. Baldridge, P. L. McCarthy and F. Urbach. (1951) *J. Amer. med. Ass.*, **146**, 1410.

The value of the diagnostic technique devised by Tzanck was confirmed. Cases of herpes simplex, herpes zoster and varicella show apparently identical epithelial cell changes which do not occur in any other vesicular skin eruption (smallpox, vaccinia, etc.). A. J. R.

NODULAR NON-SUPPURATIVE PANNICULITIS (WEBER-CHRISTIAN DISEASE). J. L. Eisaman and L. A. Schneider. (1951) *J. Amer. med. Ass.*, **146**, 1417.

The report of a single case. The authors suggest that the disease is allergic in nature with trauma as a localizing factor. A. J. R.

IMPROVED TECHNIQUE FOR DIAGNOSING RINGWORM INFECTIONS AND MONILIASIS. A. M. Kligman, D. M. Pillsbury and H. Mescon. (1951) *J. Amer. med. Ass.*, **146**, 1563.

A new modification of the Hotchkiss-McManus stain has been found useful in the direct examination of skin and nail specimens for mycelium. The method was found to be superior to the potassium hydroxide technique, giving a higher percentage of positive diagnoses. A. J. R.

CHRONIC VITAMIN A POISONING. G. Bair. (1951) *J. Amer. med. Ass.*, **146**, 1573.

A child, aged 28 months, received 240,000 units of vitamin A daily for 3 months as the result of a misunderstanding about dosage. The clinical picture included itching of the back and arms and painful swellings of the left foot, right forearm and the temporal regions. On x-ray examination hyperostosis could be demonstrated in these areas with some contiguous soft tissue swelling. There was complete recovery on stopping the vitamin A. A. J. R.

COLLECTING SPECIMENS FOR THE LABORATORY DEMONSTRATION AND ISOLATION OF FUNGI. L. Ajello. (1951) *J. Amer. med. Ass.*, **146**, 1581.

A pathologist gives advice on the collection of specimens, the method of packing and despatching them by post and suitable media for the demonstration and isolation of fungi. A. J. R.

THE VDRL TUBE FLOCCULATION TEST. T. M. Vogelsang and Rina Haaland. (1951) *Brit. J. vener. Dis.*, **27**, 52.

The VDRL tube flocculation test has proved to be a very useful diagnostic test for syphilis. In comparative investigations in 15,416 sera, with the Wassermann reaction, a complement fixation test with cardiolipin antigen, and the Meinicke clarification test, the VDRL tube flocculation test was found to have a satisfactory sensitivity and a very good specificity All the reagents in the test are standardized, and in a serological laboratory with good equipment the test can be rapidly and easily carried out. A strong point in favour of the test is that the difference between "negative" and "positive" results depends only slightly upon the personal judgment of the investigator. W. G. A.

RADIOLOGY IN SYPHILIS. K. Harvey Gaskell. (1951) *Brit. J. vener. Dis.*, **27**, 59.

The majority of the features encountered in syphilis as seen by a practising radiologist are briefly summarized, and the value of the article is greatly enhanced by numerous reproductions of skiagrams. Differential diagnosis is adequately dealt with, and the author stresses the importance of obtaining penetrating skiagrams for the proper structural demonstration of dense bone. He points out that it is the pattern, and not the density, of altered bone which gives the better clue to diagnosis between bone infection, constitutional abnormalities, and neoplasms. Attention is drawn to the fact that in the lungs, the alimentary tract, the liver and the kidneys, etc. syphilis is seldom recognized during life, either clinically or radiologically, but that it most certainly occurs and routine consideration of this possibility in differential diagnosis would undoubtedly bring more cases to light. W. G. A.

AORTITIS IN BEJEL: A PRELIMINARY REPORT. F. Akrawi and G. F. Rahim. (1951) *Brit. J. vener. Dis.*, **27**, 95.

The authors describe three cases (7·5%) of uncomplicated aortitis in a series of forty cases of late and late latent bejel, in the second decade of infection onwards. Modern radiological methods of investigation were employed, and they intend to investigate a further series of cases using similar methods and to report on them in due course. W. G. A.

SURFACE ACTIVE AGENTS IN DERMATOLOGY. R. Douglas Sweet. (1951) *The Practitioner*, **167**, 53.

This article should be consulted in the original. It catalogues the emulsifying agents dividing them into groups as follows: *Anionic*, comprising soaps, higher fatty alcohols, sulphonated fatty alcohols, sulphonated vegetable oils, sulphonated amides, alkyl aryl sulphonates and sulphonated esters of non-fatty alcohols. *Cationic*, comprising cetrimide, etc. *Non-ionic*, glycerol and glycol monoesters. The author discusses the advantages and drawbacks of the various types. A. C. R.

AUREOMYCIN: ITS TOPICAL USE IN SOME SKIN DISEASES. Bethel Solomons, Jr. (1951) *Brit. med. J.*, **2**, 525.

Aureomycin hydrochloride ointment (3%) in a petrolatum and wool-fat base was used in a heterogeneous group of infective skin conditions, including sycosis barbae, folliculitis of other areas and impetigo. It was found to have low sensitizing powers and a striking performance in healing chronic pyogenic lesions. The conclusion reached was that, at the moment, aureomycin is the best available anti-biotic in ointment form for pyogenic infections. The ointment is simple to apply and is stable over a long period without refrigeration. B. A. T.

TREATMENT OF SOME BULLOUS ERUPTIONS WITH AUREOMYCIN AND CHLORAMPHENICOL. F. Ray Bettley and E. A. Fairburn. (1951) *Brit. med. J.*, **2**, 326.

The authors point out that other workers have not been uniformly successful in treating pemphigus vulgaris with aureomycin. Diverse responses were similarly observed in the treatment of dermatitis herpetiformis. A small series is here presented of 3 cases of pemphigus vulgaris, 2 cases of pemphigus vegetans, 1 case of pemphigus erythematosus and 2 cases of dermatitis herpetiformis. In the pemphigus vulgaris cases a complete or partial abolition of fresh bullae quickly ensued upon the exhibition of aureomycin. In one the eruption was completely abolished, in the second the eruption was controlled by aureomycin, but in the third the patient died of toxaemia and exhaustion, vomiting possibly preventing retention of the aureomycin in the stomach. Chloramphenicol was ineffective in the one case treated with it. In the pemphigus vegetans cases chloramphenicol appeared to be effective in rapidly melting away the vegetating masses. In one of these cases aureomycin was ineffective in the dosage given. The 2 dermatitis herpetiformis cases showed improvement within a few days of the institution of aureomycin therapy. Although an early response to treatment may be obtained, the conclusion is reached that the anti-biotics need to be continued for at least a month or six weeks if early relapse is to be avoided, and the suggestion is made that the unsuccessful trials of these drugs may have been due to too small a dosage or too short a period of treatment. B. A. T.

ACTH AND CORTISONE IN DERMATOLOGY. Mm. Huriez, Dusausoy, Gaudier, Hochart and Lebeurre. (1951) *Bull. Soc. Franç. Derm. Syph.*, **3**, 249.

The importance of eosinophilia in dermatitis herpetiformis suggests that agents which diminish eosinophils might benefit this condition. In 4 cases the authors did not observe any spectacular action from ACTH or cortisone, but did apparently cure three cases by alternating courses of ACTH and aureomycin. They also noted some improvement with ACTH in a case of mycosis fungoides and temporary improvement in a chronic flexural eczema, in a gold rash, and some paling of the lesions in chronic lupus erythematosus, but variable results in psoriasis; cortisone was less effective. Several cases showed exacerbations of secondary infections. F. F. H.

PSEUDO-ACANTHOSIS NIGRICANS. H. O. Curth. (1915) *Ann. Derm. Syph.*, **78**, 417.

Under this term is described a condition simulating true acanthosis nigricans which occurs in obese people. It involves the axillae, neck and upper thighs but not the mucous membranes; there may also be reticular papillary lesions between the breasts. The course is benign, but at times a certain diagnosis can only be made after prolonged observation. F. F. H.

EHLERS-DANLOS SYNDROME. J. Gadrat and A. Bazex. (1951) *Ann. Derm. Syph.*, **78**, 430.

The authors report two cases and define the essential clinical features; these are fragility of the skin giving rise to the characteristic pseudo-molluscoid scars, cutaneous hyperelasticity, and over-extensibility of joints. The tendency to cutaneous haemorrhages is only a secondary and inconstant sign. The cutaneous lesions depend more on rarefaction and hypotonicity of the collagen than elastic hyperplasia. F. F. H.

ORAL ADMINISTRATION OF CORTISONE IN A CASE OF ERYTHEMA NODOSUM. A. L. Ureles and R. B. Kalmansohn. (1951) *New Engl. J. Med.*, **245**, 39.

A case of erythema nodosum which responded promptly to 100 mg. of cortisone twice daily is reported. When the dose was reduced the symptoms increased and vice versa; 75 mg. daily was given for three weeks and treatment then discontinued, since when the patient has remained well (for two months). A. D. P.